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ON THE NATURE OF THE OCULAR FLUIDS II. THE HEXOSAMINE CONTENT*

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A few years ago we isolated from bovine vitreous and aqueous humor a polysaccharide acid which we named hyaluronic acid.[1] Hyaluronic acid is composed of acetylglucosamine and glucuronic acid, and has a high molecular weight. We also isolated it from Wharton's jelly of human umbilical cord.

Hyaluronic acid occurs in bovine vitreous humor in viscous and less viscous forms as Friedenwald demonstrated (personal communication). From the apparent absence of hyaluronic acid in the blood stream we concluded that the ocular fluids could not be a dialysate of the plasma but must be formed at least in part by a secretory process, probably of the ciliary epithelium. The same conclusion has been reached by a number of other investigators, past and present, although we believe that the actual demonstration of a specifically secreted substance furnishes the only direct proof. Duke-Elder, after defending the dialysis theory for many years, has now, in a very recent article[2] accepted the theory of the secretory origin of this fluid.

Obviously a great many ophthalmological problems are connected with the production and removal of this substance in the eye, the most important probably being the mechanism of primary glaucoma.

In this paper is presented a preliminary report on some of the problems we are studying. These include a study of the hexosamine content of the aqueous and vitreous humor in different species, the hexosamine content of primary and secondary aqueous in cats and rabbits, its modification under the action of some drugs, and, finally, the hexosamine content of the aqueous humor in glaucoma.

Unfortunately the concentration of hyaluronic acid is too low for isolation or estimation in individual eyes. The next best method would be the estimation of glucuronic acid, since the serum contains no detectable quantities of glucuronic acid, and the vitreous none besides hyaluronic acid. However, the quantities of material required for the estimation of this substance are too high to be considered in our problem. We, therefore, developed a method for the estimation of hexosamine which would meet our requirements. The method is specific, as far as we know, is accurate enough for our purposes, and can be carried out easily in a large series. The method[3] had to be modified slightly to permit the estimation of the hexosamine in 0.15 to 0.20 c.c. of aqueous humor.

The hexosamine in the aqueous and

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vitreous humor may come from two sources, hyaluronic acid or serum protein. It was observed that the hyaluronic acid isolated from normal bovine eyes accounted for almost all of the hexosamine content. Recently the acid was also isolated from pig vitreous humor in a yield corresponding to 90 percent of the total hexosamine present (unpublished). This recovery is of especial interest to us since it indicates that the protein present in the normal vitreous apparently does not contain any hexosamine; that is, the normal serum mucoid or serum globulin, if present at all, is in concentrations too low for detection. In cases of increased protein content or contamination with blood, the hexosamine content is no longer an index

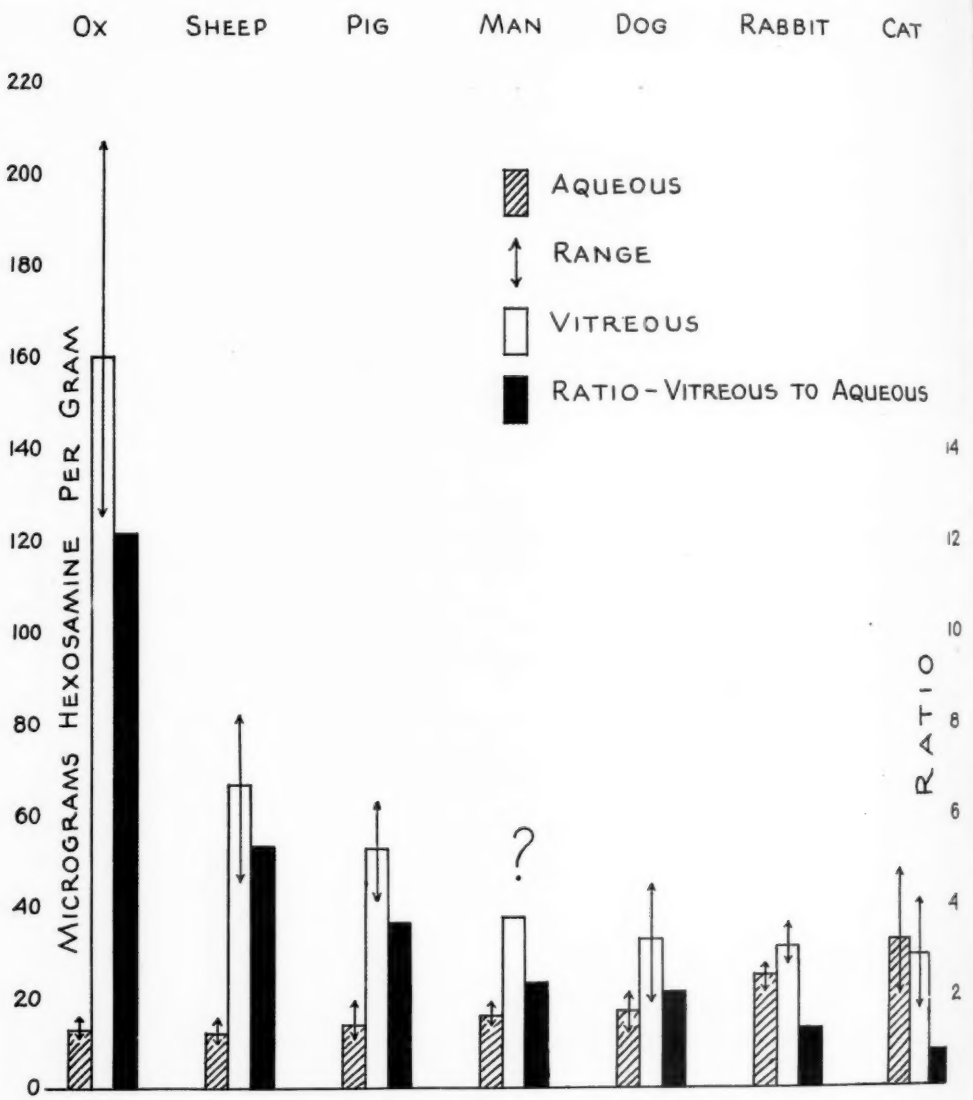

Fig. 1 (Meyer and Smyth). Hexosamine content of the ocular fluids in various species.

of hyaluronic acid. Hexosamine occurs in serum in considerably larger quantity than in aqueous humor.[3] In the former it is strongly bound in the mucoid and globulin fractions.

Hexosamine content of the ocular fluids of different species

In the present study of the hexosamine content of aqueous and vitreous humor of different species, the aqueous was obtained by puncture with a 27-gauge needle; the vitreous of freshly killed animals was obtained either by aspiration with a large needle or by dissection, and was filtered. Both methods gave identical results. The results of this study are given in table 1 and figure 1.

TABLE 1

Hexosamine content of the ocular fluids of different species

Species	Number of Eyes	Average Hexosamine in Aqueous	Range of Individual Eyes	Average Hexosamine in Vitreous	Range of Individual Eyes	Average Ratio Vitreous to Aqueous
		micrograms per gram	micrograms per gram	micrograms per gram	micrograms per gram	
Ox	11	13.3	11.9–15.5	160.0	125.7–206.5	12.1
Sheep	9	12.6	10.5–15.5	66.6	46.0– 81.8	5.3
Pig	11	14.3	11.1–19.4	52.3	41.6– 63.1	3.6
Man	5*	16.0	14.9–18.3	37.3	—	2.3
Dog	6	16.7	12.5–20.7	32.6	19.7– 44.3	2.1
Rabbit	5	24.7	21.7–26.7	31.0	28.0– 35.8	1.3
Cat	11	32.5	20.8–47.3	28.8	17.4– 40.5	0.8

* 5 samples of aqueous, 1 sample of vitreous.

This table shows the remarkable difference in the hexosamine content, especially of the vitreous humor, of different species. The ratio of the hexosamine content of the vitreous to the aqueous is apparently typical for the species. Thus the ratio in cattle eyes is 12.5 to 1, in cats it is only 0.8 to 1. We have no corresponding values for normal human aqueous and vitreous. In the vitreous of one normal case and one case of simple glaucoma the hexosamine contents were 37.3 and 31.8 micrograms per gram, respectively.

The only hexosamine-containing compound of normal aqueous and filtered vitreous humor is hyaluronic acid, as we stated before. We base this on the fact that the hyaluronic acid isolated from cattle and pig vitreous and from cattle aqueous accounts for about all of the hexosamine determined by direct analysis.

We do not know by what mechanism hyaluronic acid is concentrated in the vitreous humor, especially in species with a high ratio, such as cattle and sheep. It might possibly be that the hyaluronic acid-splitting enzyme found by us in the ciliary body[4] hydrolyzes the substance in the aqueous after it has been formed and thus accounts for the difference in concentration. This question will be studied further.

Hexosamine content as influenced by various drugs (with Doctor Gallardo)

The hexosamine content is constant and typical for both eyes of one individual. This was noted in all animals.

In table 2 are shown some of our determinations of hexosamine in the primary aqueous from the left and right eyes of cats. Cat A in this table shows a constantly lower hexosamine content than cat B.

In secondary aqueous humor, as was to be expected, the hexosamine content

increases to a variable degree with the protein content. Whether the increase in hexosamine content is due partly to an increased hyaluronic-acid content we have at present no way of determining.

TABLE 2

NORMAL VARIATION IN HEXOSAMINE CONTENT OF CAT AQUEOUS HUMOR

	Hexosamine Content in Micrograms per Gram		
	0 days	3 days	10 days
Cat A., left eye	22.2	23.4	21.7
Cat A., right eye	23.8	22.7	23.2
Cat B., left eye	31.0	39.6	36.7
Cat B., right eye	30.1	34.7	35.1

The next experiments were undertaken to determine whether certain drugs influencing autonomic innervation had any effect on the hexosamine concentration of cats' and rabbits' aqueous. In cats general anesthesia with pernostan, in rabbits local pantocaine anesthesia were used.

In table 3 the first series shows that there is no sympathetic influence on the hexosamine content of the aqueous of the second eye after one eye had been tapped. In the second series two drops of a 1-percent eserine-salicylate solution were instilled into one eye. In this series we find a significant increase in hexosamine, especially when comparing the average results of the second series with those of the third (atropine treated) and the fourth (dionin treated). The difference was noted after 20 minutes and remained constant up to 5 hours. An increase in hexosamine was always accompanied by an increase in protein concentration as estimated by increased turbidity on acidification. Not all rabbits responded to eserine with a significant increase in the hexosamine content of the aqueous, but on repetition of the experiments a few days later the same rabbits showed the same response.

In the third series of experiments 3-percent atropine sulphate showed on the average no influence on the hexosamine content. The average hexosamine content of atropine-treated rabbit eyes falls within the control range; however, some individuals responded with definite increases or decreases well beyond the control range.

In the fourth series 5-percent dionin hydrochloride was instilled into one eye. The experiments show no influence of the drug on the eye. The dionin experi-

TABLE 3

HEXOSAMINE CONTENT OF RABBIT AQUEOUS HUMOR AS INFLUENCED BY DRUGS

	Average	Range
	micrograms per gram aqueous	
1. Ten *normal* rabbits (20 eyes)	31.1	24.2 to 43.8
Difference between the two eyes of above rabbits	2.4	0.2 to 4.5
Difference between the eye used first and the eye used second	−1.6	−4.5 to +4.4
2. Control eyes of 13 rabbits	26.7	16.9 to 34.8
Eserine-treated eyes of above 13 rabbits	48.6	25.0 to 68.4
Difference between normal and treated eye	+14.6	+0.3 to +39.6
3. Control eyes of 8 rabbits	28.4	20.3 to 39.6
Atropine-treated eyes of above 8 rabbits	29.3	19.1 to 40.3
Difference between normal and treated eye	+0.8	−12.2 to +20.0
4. Control eyes of 5 rabbits	29.7	25.2 to 37.4
Dionin-treated eyes of above 5 rabbits	27.2	22.3 to 36.6
Difference between normal and treated eye	−2.5	−4.6 to +1.3

ments may be considered as a control and exclude the possibility that a local irritation was responsible for the observed changes in the hexosamine content of the aqueous.

In figure 2 we have tabulated all experiments with drugs and their controls. Each black column represents the difference in micrograms of hexosamine per gram of aqueous between the two eyes of individual animals, the difference being either positive or negative. It is evident that the increase in the hexosamine content in the eserine experiments is real. Essentially the same results were obtained in cats as in rabbits. A discussion of the meaning of such experiments has to take into account a number of factors,

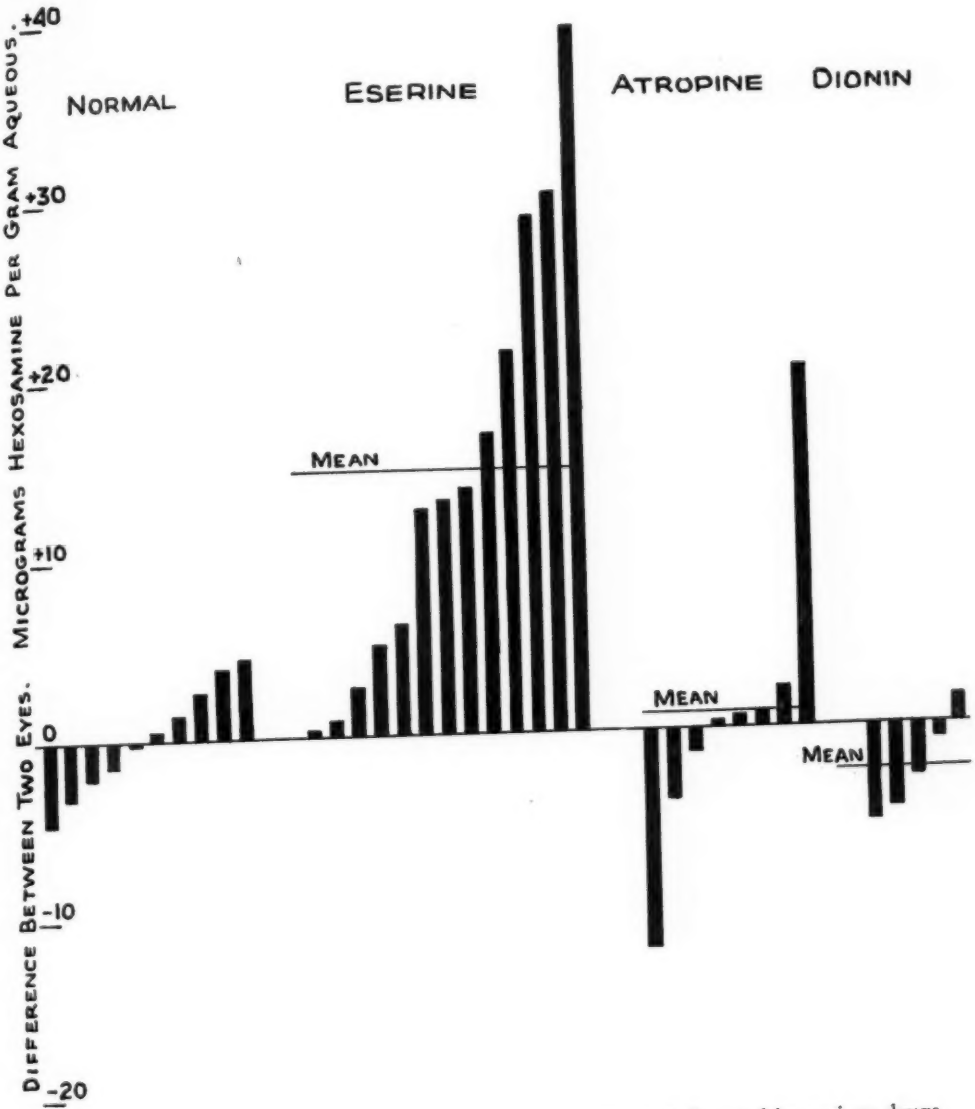

Fig. 2 (Meyer, Smyth, and Gallardo). Hexosamine content as influenced by various drugs.

TABLE 4

CONTROLS

Name	Sex	Age	Diagnosis	Hexosamine in Aqueous
				micrograms per gram
H. B.	M	28	keratitis	14.9
T. T.	M	46	senile cataract	16.3
D. H.	M	74	cataract, arteriosclerosis	15.5
J. H.	M	67	senile cataract	14.9
M. M.	F	59	cataract	18.3

such as the increase or decrease in the production of aqueous and of hyaluronic acid, and the influence of the drug on the permeability of the capillaries and the influence on the removal of the fluid and disposal of hyaluronic acid and other hexosamine-containing constituents. In the case of eserine we are inclined to assume that the increase of hexosamine is due to an increased permeability of the capillaries, since in all instances of higher hexosamine content we found an increase in protein content. If, in the human eye, eserine should cause a similar increase in hexosamine and protein content, this may explain the failure of eserine to lower the tension in some cases of glaucoma. This work will be continued with the object of finding a miotic without action on the capillaries.

EXPERIMENTS ON HUMAN SUBJECTS

We have also started hexosamine determinations of human aqueous and vitreous humor, with the object of studying primary glaucoma. Our data are still very scanty, especially on the vitreous humor, which, obviously, is difficult to obtain as material for study.

In table 4 the hexosamine content of some presumably normal aqueous humor is given. The average is 16.0 micrograms per gram of aqueous. The hexosamine concentration of one normal vitreous (from an eye enucleated for extraocular orbital tumor) was 37.3. The ratio between aqueous and vitreous humor is probably somewhat larger than two; that is, it falls between pig and dog.

In table 5 are shown data on the aqueous humor of patients with chronic simple glaucoma. The average hexosamine content of glaucomatous eyes is higher than the controls, 21.0 as compared to 16.0. The increase is small, to be sure, but whereas in the control group only one out of five is over 18 micrograms, in this group seven out of nine are over 18 micrograms. Yet there is certainly no direct correlation between ocular tension and hexosamine content, and, therefore, with hyaluronic acid or protein. For example,

TABLE 5

SIMPLE GLAUCOMA

Name	Sex	Age	Diagnosis	Tension	Hexosamine in Aqueous
				mm. Hg	micrograms per gram
R. T.	M	37	chronic noncongestive bilateral glaucoma	*37*	17.8
B. G.	M	56	chronic noncongestive bilateral glaucoma	22–27 (O.D.)	19.6
B. G.	M	56	subacute attack	*56* (O.S.)	17.3
H. Z.	M	61	chronic noncongestive glaucoma	26–37	20.3
L. R.	F	65	chronic noncongestive glaucoma	35	19.1
S. Ma.	F	68	absolute glaucoma, cataract extraction 3 years ago	*34*–75	31.0
H. P.	F	46	suspected glaucoma, not verified; glaucoma in family	20	20.1
J. F.	F	65	chronic noncongestive bilateral glaucoma; bilateral secondary cataract; acute attack	55–*too high to read*	22.5
C. R.	F	69	primary glaucoma; two trephine operations, cataract extraction; enucleation	43–60	21.5

in the second case, the hexosamine content of the aqueous of the right eye was 19.6 when the tension was low, but was only 17.3 in the left eye when the tension was high (56 mm. Hg). Even in the aqueous of patient J. F., which Doctor Kirby obtained during an acute attack, the hexosamine was not much above the normal range. Only in one case, S. Ma., was a high value found (31 micrograms), when the tension at the time of taking the sample was 34 mm. Hg.

If we take into account the fact that most of these eyes were eserinized, the apparent elevation becomes still less significant. The conclusion we wish to draw from our experiments at this time is only a negative one; namely, that there is no relation between the increase in hyaluronic acid and protein and ocular tension in primary simple glaucoma, not even in the one case of an acute attack. It seems of importance to stress the absence of an elevation of the protein content in the aqueous. This finding seems to us to exclude histamine as the cause for the increase in the tension, a theory proposed by Friedenwald[5] and later by Duke-Elder,[6] since histamine should increase the protein content and with it the hexosamine content of the aqueous by increasing the permeability of the blood vessels.

We were able to obtain vitreous from only one case of primary glaucoma, case C. R. The vitreous, obtained immediately after enucleation of the eye by Doctor Wheeler, was under a high tension. It showed a low hexosamine and protein content (21.5 micrograms hexosamine and 78 micrograms protein nitrogen per gram). This hexosamine content is lower than that of the vitreous of a normal eye enucleated from a young girl by Doctor Wheeler for extraocular orbital tumor. The total nitrogen was apparently not increased.

In secondary glaucoma the hexosamine content, and, as would be expected, the protein content of both aqueous and vitreous were found to be high. In two eyes the hexosamine contents of the aqueous (taken after enucleation) were 56.6 and 73.9 micrograms per gram, respectively; of the vitreous, 76.0 and 94.9 micrograms. The values for protein nitrogen were 878.0 and 956.0 micrograms per gram; that is, the hexosamine content is 2 to 3 times as great and the protein content more than 10 times as great as in primary glaucoma.

The results we have obtained so far seem to warrant the pursuit of this line of investigation. We believe that the polysaccharide acid of the ocular fluids, its

TABLE 6
ENUCLEATED EYES

Name	Sex	Age	Diagnosis	Hexosamine in Aqueous	Hexosamine in Vitreous	Total N.* in Vitreous	N.P.N.† in Vitreous	Protein N.‡ in Vitreous
				micrograms per gram	micrograms per gram	micrograms per gram	micrograms per gram	micrograms per gram
D. S.	F	7	extraocular orbital tumor	—	37.3	235.0	—	—
C. R.	F	69	absolute primary glaucoma	21.5	31.8	250.0	172.0	78.0
S. M.	M	52	secondary glaucoma	56.6	76.0	1124.0	246.0	878.0
S. C.	F	57	secondary glaucoma	73.9	94.9	1180.0	224.0	956.0

* Total nitrogen determined by microkjeldahl method, on filtered vitreous.
† Nonprotein nitrogen determined on trichloracetic filtrate, by microkjeldahl method.
‡ Protein nitrogen calculated by difference.

production and removal, play an important part in the pathology of the fluid exchange of the eye. It may take a long time before anything is known about this complicated mechanism, but there apparently is no short cut to the solution of this problem, and only slow and cumbersome quantitative analyses and the elaboration of yet more specific and quantitative methods give any promise of success.

I should like to outline another phase of the study of hyaluronic acid, opening up a field of research not only of importance to ophthalmology but to other fields of medicine. Kendall, Heidelberger, and Dawson isolated a polysaccharide acid similar to ours from young mucoid cultures of hemolytic streptococcus.[7] We were able to demonstrate the identity of this carbohydrate with ours. An enzyme preparation, obtained by Dubos[8] from autolyzed pneumococci specifically hydrolyzed these substances, the reaction kinetics being identical.[4] The same enzyme was found by us in suspensions of ciliary body and iris. It was shown recently by Loewenthal[9] that precipitating sera of high titer against the polysaccharide acid can be obtained by immunizing rabbits with carefully killed young cultures of hemolytic streptococci. This quite strange relationship of these polysaccharide acids and their corresponding enzymes is perhaps still more emphasized by our isolation from synovial fluid, within the past few months, of a polysaccharide acid resembling hyaluronic acid in all respects.[10]

It is a temptation to link some manifestations of hemolytic streptococcal infections to the occurrence of one and the same carbohydrate in the coccus and in the affected organs.[11] This will be another problem for future research.

Before closing we wish to thank Dr. John M. Wheeler for the help and encouragement we received during this work. Our thanks are likewise due to the other surgeons of the Eye Institute who gave us material with which to work, and especially to Dr. Daniel B. Kirby, who obtained for us most of the human aqueous humor reported on in this paper.

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INFLUENCE OF DINITROPHENOL ON THE PRODUCTION OF EXPERIMENTAL CATARACTS BY LACTOSE*

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Because of the clinical reports that administration of dinitrophenol to patients had been followed, in some instances, by development of cataracts, studies were undertaken to elucidate the possible role, if any, of dinitrophenol in this clinical syndrome. It was realized at the outset that no very obvious relationship of cause and effect was likely to be found, since exposure of large numbers of workmen to dinitrophenol in munitions plants during the World War had apparently not resulted in cataracts. Furthermore, extensive studies in this and other laboratories, where dinitrophenol had been administered to almost all the common laboratory animals under a variety of acute and chronic conditions, had never resulted in any demonstrable pathological changes in the eyes. For instance, white rats, which are generally susceptible to cataract production, had been fed up to fatal concentrations of dinitrophenol in their diets continuously from the time of weaning until death (at the end of about two years) without showing the slightest deviations from normal in their eyes and lenses.[1]

More direct studies of the effects of the drug on the lens metabolism were made by Field et al,[2] in which they showed that, both qualitatively and quantitatively, the metabolism of the lens responded to dinitrophenol in substantially the same manner as do other tissues. Thus, there was no basis for considering some aberrant form of metabolic change from the drug in the lens. It was also shown in another paper[3] that the permeability of the lens capsule was not changed *in vitro* or *in vivo* by dinitrophenol. Finally, the hypothesis was tested[4] that vitamin deficiency, such as might be present in patients attempting weight control, could predispose the lens to formation of cataract through the administration of dinitrophenol, but with entirely negative results. Therefore, it seemed improbable that any of these mechanisms could be concerned with the clinical cataracts reported after dinitrophenol.

Another possible approach to this problem was to put experimental animals under conditions which, in themselves, produce cataracts, and to determine whether administration of dinitrophenol would accelerate production of the cataracts, produce an increased incidence, or more rapid or complete progression. That is, dinitrophenol might conceivably affect, in some way, an active or latent cataractous process. The present paper deals with the experimental results obtained along these lines.

Methods

The method of Mitchell and Dodge[5] afforded a satisfactory way of producing experimental cataracts; that is, by feeding large amounts of lactose to white rats in their diets. The method, as adapted to the present study, was to put young littermate rats weighing 40 grams on an experimental diet, which was continued for 180 days, or until they died. They were divided into paired cages, containing 5 or 6 rats each, and received the same diet.

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except that those in one cage of each pair received food medicated with 0.075 percent of alpha dinitrophenol (1-2-4). The dinitrophenol was put in as an alkalinized solution, and mixed in a mechanical mixer in order to obtain even distribution of the drug.

The rats were not segregated by sex, although they bred on these diets only very rarely. When a litter was born in the experimental cages, the young were immediately removed, but the mother was kept under the experimental conditions, so that we might observe whether the pregnancy had altered the course of her response to the conditions. Since the responses of male and female rats were indistinguishable, and females were not affected by pregnancy, the results have been considered together in an analysis of the data.

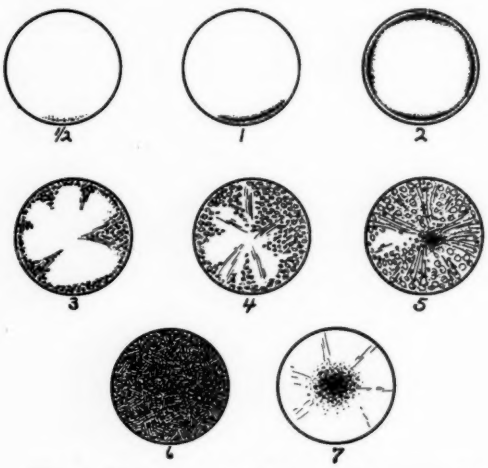

Fig. 1 (Borley and Tainter). Diagrammatic representation of stages of cataract production by lactose in white rats. Stage ½: Earliest change detectable with ophthalmoscope, without complete opacity at any point. Stage 1: First area of complete opacity (usually a crescent at equator). Stage 2: Extension of crescent to involve all or practically all the equatorial region. Stage 3: Extension of opacities towards center, but covering less than one third of lens area. Stage 4: Further extension of opacities to cover between one third and two thirds of lens area. Stage 5: Further extension of opacities to cover more than two thirds, but not the entire lens surface. Stage 6: Lens completely opaque (mature cataract). Stage 7: Liquefaction with opaque nucleus floating in lens sac (hypermature cataract).

The diet consisted of 15-percent crude casein, 4-percent Osborn and Mendel's salt mixture, 9-percent hydrogenated vegetable oil (Crisco) and 2-percent cod-liver oil. The remainder of the diet was carbohydrate, consisting either of 70-percent lactose U.S.P. or lesser proportions of lactose, the total being made up with cornstarch. In the beginning the yeast requirement was met by adding 4-percent irradiated brewer's yeast to the diet. However, none of 24 adult rats fed on this diet with up to 70-percent lactose, showed any changes in the eyes in 3½ months. When young rats of 20 to 40 gm. were given this same diet, they died too rapidly for cataracts to be produced. Thinking that part of the difficulty might be an inadequate intake of yeast, the concentration was raised to 10 percent, but with the production of only very marked diarrhea, emaciation, and too early death for the purposes of the present study. Therefore, all these preliminary experiments were discarded in the ultimate evaluation of the results. Finally, a satisfactory routine was established by feeding separately 0.5 or 1.0 gm. of yeast moistened with a drop of cod-liver oil daily to each individual rat. The weights of the animals were recorded thrice weekly, and food and water consumption were measured at the same time. Both eyes of each rat were examined daily for cataractous changes during the first month, the interval between the examinations being gradually lengthened until one examination weekly was made in the sixth month of the experiments, when the changes were very slow. Examination of the eyes consisted of ophthalmoscopic study of the lenses for opacities, together with confirmation of the crucial findings by slitlamp microscopy. When opacities developed, they were recorded

as to appearance and magnitude of the changes by reference to an arbitrary standard of stages, based on the amount of opacity. In figure 1 are depicted schematically the various stages of these cataracts, showing the complete cycle of development from the earliest change (stage ½) to the hypermature cataract (stage 7).

Stage ½ was defined as comprising the earliest changes that could be detected with the ophthalmoscope, consisting of some beginning lack of translucency of the lens at one point in its equatorial region. This was readily visible through the thin transparent iris without dilatation of the pupil. Slitlamp examination at this stage showed early vacuolation of the subcapsular fibers of the cortex in the equatorial region, associated with fine striate opacities of the capsule and subcapsular cortex in the anterior polar portion of the lens, the latter not being recognizable with the ophthalmoscope. No visible nuclear changes were present. Stage 1 represented the development of the first area of complete opacity, which appeared, when observed with the ophthalmoscope, as a small black crescent occupying a portion of the equatorial region or periphery of the lens. The cataract was taken to have reached stage 2 when the crescent extended around the entire equatorial region. In stage 3, the circumferential band of opacity had begun to extend towards the center, but covered less than one third of the total lens area, as seen by anterior illumination. When seen with the slitlamp, the opacities at this stage were localized mainly in the anterior cortical layers, and consisted of further fine vacuolation of the lens fibers interspersed with fine linear opacities of the cortex and capsule extending in a radial direction. At this stage, better definition of the nucleus was also observed with well-defined anterior and posterior Y formation. This refractive change in the nucleus could not be seen with the ophthalmoscope.

In stage 4, the opacities had increased to such a degree that between one third and two thirds of the lens was opaque, and in stage 5, over two thirds but not all of the lens was involved. In stages 4 and 5, when observed with the slitlamp, the vacuolation of the lens fibers appeared more pronounced, the vacuoles coalescing to form larger ones, although fewer in number in the cortex, and extending towards the center. The linear opacities became much more pronounced and numerous, and were seen to involve the cortex to a greater depth. The nuclear changes were visible in stages 4 and 5 before complete opacification of the cortex, and simply consisted in a denser cloudiness of the area with obliteration of the lens Y figures. In stage 6, the entire cortex of the lens was opaque to the ophthalmoscope, representing the clinical stage of maturity. At this stage the lens of the rat appeared as a white opaque disc recognizable even from a distance on casual examination. With the slitlamp, however, nuclear changes were obliterated by the complete opacification of cortex. Finally, stage 7 demonstrated the hypermature cataract, in which degeneration and liquefaction of the entire cortex had taken place, and the opaque nucleus was seen to be floating eccentrically in a sac of liquid.

These stages gave a roughly quantitative method for recording the degree of pathological changes presented by the lens. It was sufficiently exact so that only very occasionally did the reading deviate by as much as one-half stage from the curve of change which the particular animal was following. The readings were frequently checked independently by a second observer, giving results which were always in close agreement with those of the usual observer. Thus, there was little difficulty in evaluating the amount and progress of the cataractous changes.

EXPERIMENTAL DATA AND RESULTS

Size of rats: Thirty weaned rats, under 30 grams in weight, were divided into 6 cages and fed the stock diet made up with 50-, 60-, or 70-percent of lactose, the animals in half the cages getting the usual dinitrophenol. These diets were too toxic for the young rats. Although a few early lens changes were observed, deaths were so frequent in the first two or three weeks that no conclusions could be safely drawn. Hence, the size of the rats for starting the experiments was set at 40 grams weight, with better results.

Diarrhea and malnutrition: A close relationship was observed between the production of diarrhea and loss of weight and time of appearance of the cataracts. In fact, all rats on these lactose diets showed a practically complete cessation of growth, with an average daily change during the experimental period of only a few hundred milligrams, either increase or decrease. The diarrhea was very marked, and the animals sat hunched up, as if suffering from abdominal discomfort.

Since there was a possibility that the diarrhea was the primary cause of the cataracts, and that the lactose and yeast acted merely as laxative agents, other cathartics were tried to see if these also would produce changes in the lenses. In one cage of 6 rats, 2-percent castor oil was fed in a normal stock diet for 2 weeks, followed by increasing concentrations of phenophthalein up to 1 percent, which was continued for 55 days. The rats seemed particularly resistant to these two laxatives, since they had a few soft stools during the first days of medication, but thereafter appeared quite normal. No changes in the eyes were observed. Repetition of the experiment with another cage of 6 rats also caused no severe degree of diarrhea or serious stunting of growth.

A final attempt to produce a chronic diarrhea was made more successfully by using powdered extract of colocynth. A concentration of 0.2 percent in the normal stock diet[4] produced moderate diarrhea, complete stoppage of growth, and death of three of the five rats in 18 days (average). Another rat died 9 days after the concentration was raised to 0.4 percent, and the last rat withstood 41 days of this concentration, followed by 21 days more of 0.8 percent. Thus, over a total period of several months, gastroenteritis, diarrhea and malnutrition were present in these colocynth-treated rats, similar in degree to that observed in the lactose-treated rats. However, in none of them was there any visible change in the lenses of the eyes. Therefore, these physical conditions by themselves were not sufficient to produce the changes in the eyes to be described later, but rather the cataracts depended on some specific action of the lactose-yeast diets.

High cornstarch diets: As a control, early in the study, a pair of cages containing 5 rats each, were set up on the regular cataract-producing diet described under *"methods,"* but with carbohydrates supplied solely as 70-percent cornstarch, without lactose. Two of the rats in the dinitrophenol cage showed changes in their lenses beginning in 6 days. In one rat, stage 2½ developed by the eighth day, followed by a gradual regression until the eyes were both normal on the 26th day. In the other rat a slight (stage 1) degree of change was present from the 6th to the 19th day after which the eyes were normal.

Thinking that this might be an indication of a toxic action of dinitrophenol on the lens, an attempt was made to repeat the results on a second group of 10 rats. Since the other control experiments had shown that a high yeast intake was indispensable, the daily yeast intake was raised to 1.0 gm. per rat for this group,

with the 70-percent cornstarch diet otherwise unaltered. Six months of this diet caused absolutely no changes in the eyes of either the dinitrophenol or the unmedicated rats. Later, a second similar attempt was made with the same number of rats, to repeat the early observation, but with completely negative results. Therefore, in 6 months of continuous feeding of 70-percent cornstarch to a total of 20 rats none of the changes observed in the two rats in the early series were observed again.

We have no explanation of the failure to obtain positive results a second time. It is possible that those early changes were caused by some intercurrent factor not related to the experimental condition, but operating independently. Evidence in favor of this possibility was that the cataractous changes occurred earlier than was customary, even with the most drastic conditions of lactose feeding, and that they regressed spontaneously, leaving the lenses normal, while the diet and dinitrophenol administration were still being continued unchanged.

Lactose 70-percent diet: Five separate groups of rats were continued on lactose 70-percent until the death of all the rats, or after 6 months time had elapsed. These groups were not run simultaneously but were nearly consecutive, so that they covered several years of experimentation. In the first four groups there were control cages of 5 or 6 rats each, and similar cages on the same diet with added dinitrophenol. In the last group, 3 different market brands of dinitrophenol were tested in separate cages against the usual control cage. There was thus a total of 5 control cages containing 26 rats, and 7 medicated groups containing 36 rats.

The earliest observed change in any of the control rats was seen on the fifth day of the experimental diet. The earliest cataract observed among all the dinitrophenol-tested rats in this group was also on the fifth day; thus these intervals were the same for the two series. In

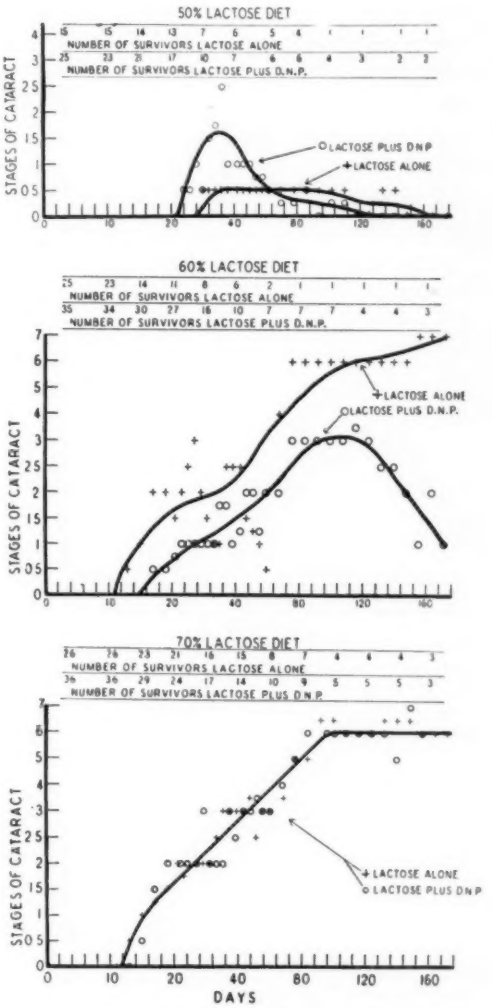

Fig. 2 (Borley and Tainter). Curves of median cataract production in white rats given various concentrations of lactose in their diets, with and without the addition of dinitrophenol (D.N.P.), 0.075 percent.

figure 2, there is depicted the median times of development of cataracts and a curve of changes with the lapse of time. Figure 2 also shows the medians at each time interval, from which a smooth curve has been drawn. Because the curves of

the dinitrophenol group did not differ from the control, a single curve represents both sets of data accurately.

It can be seen that the median time for development of the first detectable cataractous change was on the 12th to the 14th day. At that time, there had already been a considerable number of deaths among the rats, as shown by the digits above the curve. The rate of development of the cataracts was very regular, so that on the 100th day the median result was a mature cataract; that is, one in which the lens was completely opaque (stage 6). The mortality on these diets was very high, so that only 9 of an original group of 62 rats survived 100 days. Thereafter, the changes were slight and their comparative significance was further minimized by the small number of animals remaining.

The conclusion appeared justified that dinitrophenol, added to a 70-percent lactose diet, caused neither a greater incidence, an earlier onset, a more rapid development, nor a greater final degree of cataractous changes than did the diet without the drug added. Therefore, there was no demonstrable influence of the dinitrophenol on the production of cataracts, under these conditions.

Lactose 60 percent, 50 percent, and 25 percent in diet: Because the above experiments lent no support to any assumption that dinitrophenol could modify a fully effective set of cataractous conditions, a modification of the procedure was used in order to detect, if possible, the influence it might have in the zone of threshold degrees of action. Accordingly, similar groups of rats were carried through with basic diets containing 60 percent, 50 percent, and 25 percent each of lactose. It was thought that such diets would tend to induce a moderate, or perhaps not quite effective, tendency towards cataracts, and that dinitrophenol, if it had any specific action in this respect, might more readily transform this latent or incomplete tendency into a definite pathological lesion of the lens.

Only one group of 2 cages of 6 rats each was studied at the level of 25 percent. There was no indication of any pathological changes in the eyes of either the medicated or the control rats at the end of 6 months. Attention was, therefore, centered on the 50-percent level, which was practically the minimal concentration for cataracts, and the 60-percent level, which had a slightly greater effect.

Fifty-percent lactose was put in the diet of 3 groups of rats, consisting of 3 control cages of 15 rats in all, and 5 dinitrophenol cages containing 25 rats. The dinitrophenol diets seemed definitely more toxic than did the unmedicated for these rats, since at the end of 20 days, or the time when cataracts were just beginning to appear, 32 percent of the dinitrophenol rats had died as compared with only 13 percent of the control group. Similarly, the control rats gained an average of 0.72 grams per rat per day during the experimental period, whereas the dinitrophenol-fed rats increased only 0.08 grams per day.

The median time of onset of the cataracts was 30 days in the control groups, and 24 days in the dinitrophenol group. In addition, the dinitrophenol-fed rats seemed to develop cataracts more rapidly and to a greater degree until about the 60th day, when the reverse was true. In view of the fact that too few rats were surviving to permit safe conclusions to be drawn, it was felt that the discrepancies were not great enough to establish a reliable difference between the medicated and unmedicated animals. This was especially true in view of the opposite results with the group on 60-percent lactose.

Five different groups of rats were fed the standard diet made up with the 60-percent lactose, in a further effort to establish the aforementioned "threshold conditions." In the five groups there was a total of 25 control rats, divided into 5 rats for each control cage for each group, and 35 dinitrophenol-medicated rats similarly divided into 7 cages as above. In these experiments, 44 percent of the control rats had died as compared to only 14 percent of the dinitrophenol rats at the median time of onset of cataracts; that is, in 14 days. This condition was just the reverse of that manifested in the 50-percent-lactose group, and was due, in all probability, merely to random distribution of the results. Moreover, in agreement with the higher mortality, the cataracts in the control group began at a median of 13 days, as compared to 17 days, or 4 days later, in the dinitrophenol-fed rats. The control rats had cataracts that developed more rapidly than did those in the medicated rats, and the median curves showed a difference of at least one stage throughout the duration of the study.

When the results with the 50-percent and 60-percent-lactose groups were merged, the mortalities of the controls and dinitrophenol rats were practically identical. By the same procedure, the median curves of cataract changes in the lenses were substantially the same. There can be little doubt, therefore, that when due weight was given to the different variables involved, dinitrophenol did not demonstrably affect the cataractous process produced by lactose. Therefore, no evidence was obtained that dinitrophenol could potentiate an incipient or latent cataractous change into an active or more progressive change.

Dinitrophenol of different manufacturers: Because of the possibility that the dinitrophenol of some particular manufacturer might have been contaminated with some cataract-producing impurity, the dye as manufactured and supplied for clinical use by the three leading distributors of the drug was obtained and tested as outlined above. It seemed highly improbable that such impurity was the cause of the cataracts, in view of the care which these reputable manufacturers take in insuring purity of their medicinal products. Moreover, cataracts had been reported after the use of several of the common brands of the drug, and after dinitrophenol which was shown to be pure by the best available chemical tests. However, the data of this study were analyzed from this standpoint, since it contained parallel series of rats treated with dinitrophenol obtained from three different commercial sources.

With the drug from one source, the median time of development of cataracts was 16 days, as compared with 13 days for the controls; from a second source, 20 days as compared with the control of 15 days; and from a third source 15 days and 14 days, respectively. Similarly, there were no differences in the speed of development of the changes with the different lots of material, nor in the ultimate degrees of cataractous changes produced.

Therefore, no evidence was obtained to indicate any difference in the effect, or lack of it, between the dinitrophenols of three different manufacturers.

Summary and conclusions

1. In paired feeding experiments lasting up to 6 months each, white rats were given lactose-containing diets, which usually produced cataracts. One half of the rats also received 0.075-percent alpha dinitrophenol (1-2-4) added to this diet. The eyes of each rat were examined ophthalmoscopically and with a slitlamp at frequent intervals throughout. The amount of cataractous change present was

recorded in terms of a new semiquantitative scale of opacity of the lens, developed for this purpose.

2. No cataracts were produced on 25-percent lactose diets whether dinitrophenol was administered or not.

3. On diets containing 50-percent, 60-percent, and 70-percent lactose, the majority of rats showed demonstrable cataractous changes, the degree of change being proportional to the lactose content of the diet. At the 70-percent level, the cataracts became fully mature and finally liquefied, as do other types of clinical cataracts.

4. Addition of dinitrophenol to these cataract-producing diets did not alter the frequency of the median time of appearance of the cataracts, the median rate of progression, nor the ultimate magnitude of the changes.

5. Accordingly, no evidence was obtained that dinitrophenol could either speed up a preëxisting cataractous process, or render active an inactive or latent cataractous tendency.

6. No differences in these respects were found with dinitrophenol supplied by three different manufacturers.

7. The results of this, and related reports, do not show any causal relationship between cataract formation and dinitrophenol medication, and thus do not provide any explanation of clinical cataracts reported to have occurred in some patients taking dinitrophenol for weight reduction.

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[2] Field, J., Tainter, E. G., Marten, A. W., and Belding, H. S. Amer. Jour. Ophth., 1937, v. 20, p. 779.
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Discussion

Dr. T. D. Allen: So-called dinitrophenol cataracts in several of my patients were not noticed clinically until two to four months after a second series of dinitrophenol medication was started. Did you try giving the dinitrophenol over two to four months, then stop for two to four months, and then start a second time on any series of animals?

Dr. Borley: Up to the present time we have not given a series of animals dinitrophenol under those conditions. There have been several series carried up to a period of about three to four years, and in heavy doses of dinitrophenol without lactose diets, without showing any signs of cataracts.

I think possibly that that might be done in the future in view of the fact that in some of the cases, or in quite a number, apparently the dinitrophenol had been stopped, though the clinical reports on many of them showed they were taking it at the time that the cataracts developed.

Dr. S. Judd Beach: I should like to ask the essayist if there were any data on the blood or lens chemistry in these cases.

Dr. Borley: In these particular experiments we did not attempt to take any of the blood chemistry or the sugar output in the urine, any chemical data of any kind. About the only work along this line that has been done in relation to dinitrophenol has been the experiments of Dr. Field and collaborators on the relation of the dinitrophenol to consumption of the lens.

GLAUCOMA: CLASSIFICATION, CAUSES, AND SURGICAL CONTROL*

Results of microgonioscopic research

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San Francisco

Introduction

On the basis of microgonioscopic and surgical investigations the writer suggests in this paper the principal means by which increased intraocular pressure is produced in primary glaucoma and how it may be controlled. In the majority of cases, increased pressure appears to be directly due to mechanical obstruction of the circulation of intraocular fluid at some point along its course. These mechanical derangements can be visualized in the living eye by means of a method of biomicroscopy (microgonioscopy) and can be demonstrated by certain experimental procedures. Glaucoma may be classified on a mechanical-causal basis into two major anatomic entities. The mechanical characteristics of each entity are described, as well as their relief by mechanical or surgical means.

It is impossible in the limited scope of this paper to do more than mention some of the observations that have been made. Neither does space permit reference to the many glaucoma theories that have been put forward or to mention more than a few of the many names of those who have contributed to the study of this problem.

Microgonioscopic and operative methods for the study of the anterior segment in glaucoma

An improved technique of biomicroscopy of the angle including a microgonioscopic floor stand and diagnostic contact glass[1, 2] for viewing the chamber angle was employed in these investigations. The depth of the anterior chamber was measured by means of a micrometer screw attached to the corneal microscope.

In order to study the hydromechanics of the glaucomatous eye and to determine the site of obstruction to the flow of intraocular fluid, a combined surgical technique† was devised. It consists in the artificial deepening of the anterior chamber by injection of a solution of physiological saline before, during, and at the end of the operation combined with posterior sclerotomy, and occasionally, in selected cases, with aspiration of vitreous,‡ and the performing of one or of multiple excisions of the root of the iris through oblique, valvelike keratome incisions in the cornea. This procedure has proved successful for the relief of increased intraocular pressure in the shallow-chamber type of glaucoma in fifteen cases.

Deep-chamber type of glaucoma. This anatomic group covers what in the usual terminology is known as "chronic simple glaucoma." There is evidence[3, 4, 5] to show that the mechanical cause of increased intraocular pressure in this large group

* Read before the American Association for Research in Ophthalmology at San Francisco, June, 1938.

† "An operative procedure for shallow chamber type of glaucoma." Presented before the Demonstration Session, Section of Ophthalmology, A.M.A., San Francisco, June 16, 1938.

‡ The anterior chamber has been injected with physiological saline by Howard to facilitate entrance of the knife in cases of cataract and glaucoma with shallow chamber, and vitreous has been aspirated by Zur Nedden in many cases to remove opacities; without harm in both instances.

of cases of primary glaucoma is closure or obstruction of the pores of the sclerocorneal trabeculum. This type is characterized by normal depth of the anterior chamber and open iridic angle (fig. 1). Incising the trabeculum under direct vision in this type of case by goniotomy[6, 7, 8] reduces abnormally increased intraocular pressure. The explanation for this prolonged reduction of intraocular pressure (to date three years) seems to be the reëstablishment of a normal direction of outflow from the anterior chamber into Schlemm's canal.

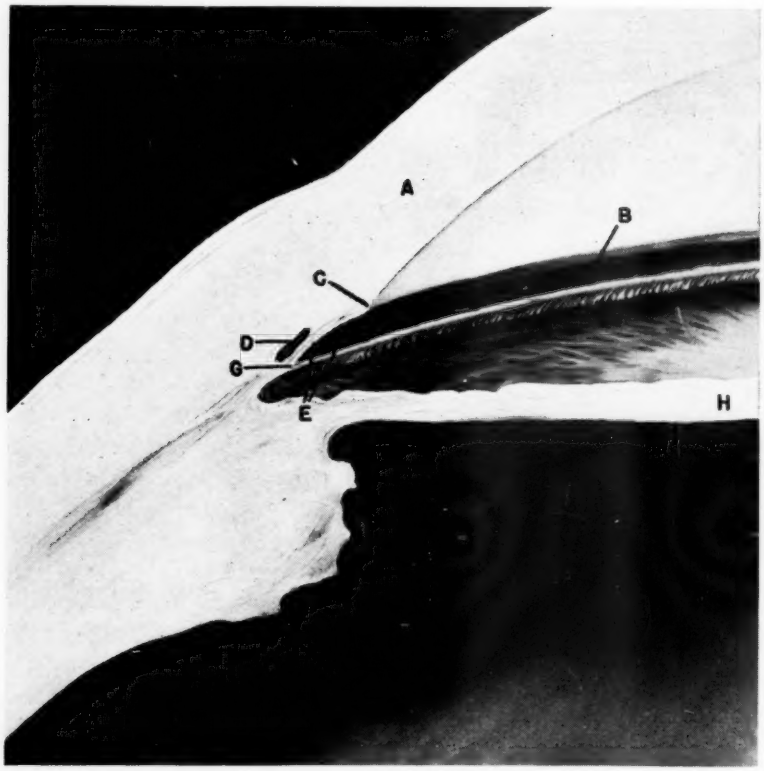

Fig. 1 (Otto Barkan). Deep-chamber type of chronic glaucoma. A, cornea; B, trabecular pigment band; C, internal annular ring of Schwalbe; D, Schlemm's canal; E, sclerocorneal trabeculum; G, scleral spur; H, iris, anterior surface.

It should be noted in this connection that it does not necessarily follow from the aforementioned facts, that mechanical blockage is the primary cause of increased intraocular pressure in this type of glaucoma. Microgonioscopic observations of obstruction of the sclerocorneal trabeculum in the shape of a pigment band or other signs of impermeability in apparently healthy fellow eyes without demonstrable increased pressure do indeed suggest that the mechanical block antedates the rise of pressure. But, on the other hand, the evidence does not preclude the possibility that the original rise in pressure is caused by physico-chemical changes which antedate and finally result in this demonstrable mechanical block. However this may be, it does not invalidate the practical, theoretical, and therapeutic importance of the fact that removal of the mechanical obstruction actually

does reduce the abnormally increased intraocular pressure in this type of glaucoma. This normal or deep-chamber type runs a noncongestive course until in enters the late stages, at which time it may become "decompensated" and appear "congestive." It is then distinguished by the normal depth of its chamber from the "congestive" attack of a case of the shallow-chamber type which has up to that time run a "noncongestive" or "simple" course.

Fig. 2 (Otto Barkan). Shallow-chamber type of chronic glaucoma. A, cornea; B, narrow slitlike entrance to the angle; C, internal annular ring of Schwalbe; D, Schlemm's canal; E, sclerocorneal trabeculum; G, scleral spur; H, iris, anterior surface.

Shallow-chamber type of glaucoma. This second anatomic group of glaucoma envelops the clinical picture known as "chronic congestive glaucoma." This type is characterized by a shallow anterior chamber and narrow entrance to the angle (fig. 2). In mydriasis the peripheral folds of the iris tend to crowd the angle. The block to filtration is at first produced by the root of the iris lying in apposition to the wall of the angle. It can be shown in successfully iridectomized cases, that the trabeculum is permeable. This type also includes certain clinically "noncongestive" cases with shallow chamber, previously mentioned. These cases in the past have often been erroneously regarded as belonging to "chronic simple or noncongestive glaucoma" because of the absence of congestive signs and symptoms. It can now be shown that these "noncongestive" cases belong to the pathologic anatomic entity of shallow-chamber and narrow-angle glaucoma and are of the same mechanical etiolgy as the "congestive" cases. By means of a mild provocative

mydriatic drop, such a clinically "noncongestive case" can be converted into a clinically "congestive" or so-called decompensated glaucoma. On the contrary, normal or deep-chamber glaucoma in which the angle is open is not thus affected by mydriatics. The correctness of this conception is further confirmed by noting the immediate reduction of intraocular pressure when the angle is set free (observed biomicroscopically). This may be accomplished either medicinally (miotics) or by surgery (basal iridectomy or iridotomy) in shallow-chamber glaucoma, provided that extensive permanent organic adhesions of the iris in the angle are not present.

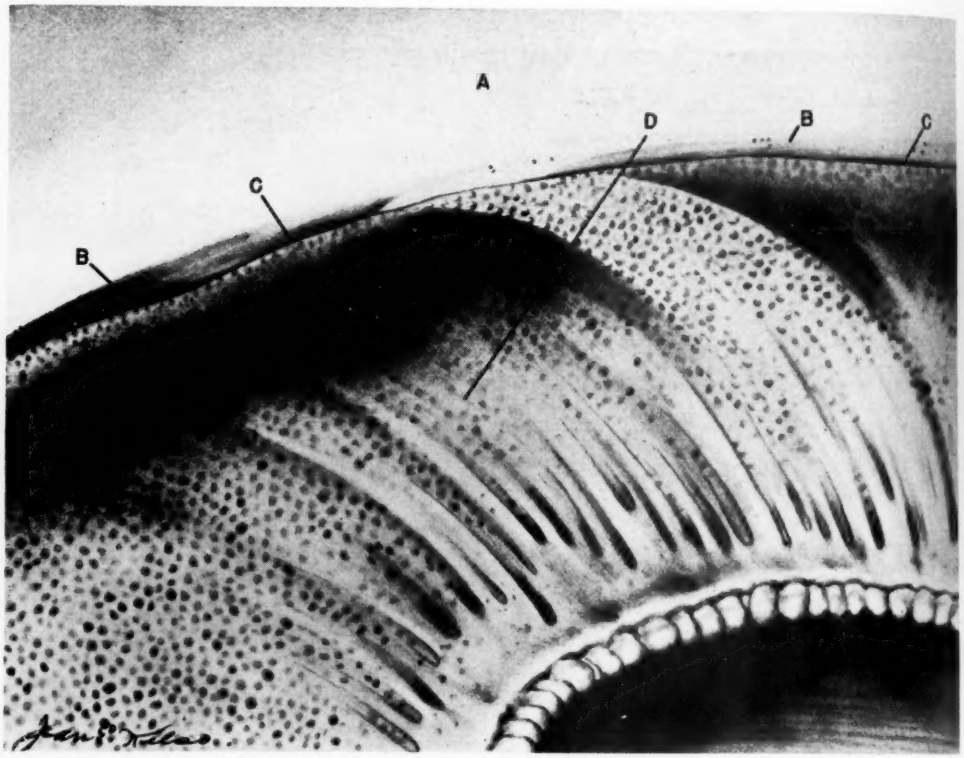

Fig. 3 (Otto Barkan). Shallow-chamber type of chronic glaucoma, showing microgonioscopic appearance of narrow entrance to angle. A, cornea; B, internal annular ring; C, slitlike entrance to angle; D, anteriorly displaced iris diaphragm.

In the shallow-chamber type, as the pupil dilates or the iris diaphragm advances, transient contacts take place between the root of the iris and entrance to the angle (internal annular ring of Schwalbe) thereby causing obstruction of outflow (fig. 3). Since the resultant increase in intraocular pressure is, under these conditions, more apt than not to be of sudden onset, it may not permit immediate adjustment in the local circulatory apparatus to the newly changed intraocular condition. If the increase in pressure is of short duration, no congestive symptoms need appear. If, however, the periods of obstruction and of increased pressure are maintained long enough and are sufficiently rapid in their rate of onset, then subjective symptoms of congestion in the form of mists, haloes, and pain may arise. These will be

accompanied by objective signs, such as venous stasis, ciliary injection, haziness of the cornea, and other evidence of "congestion" and "decompensation." If the apposition of the periphery of the iris is not soon relieved either by medication, by operation, or spontaneously, a permanent organic adhesion ensues (fig. 4). This adhesion is brought about as the result of congestive transudation and inflammatory reaction, as one may see known later stage of more or less permanent chronic congestion with venous stasis is ushered in. Prospects of successful surgery are thereby considerably reduced.

Incidental to these observations it was noted that the formation of a membrane and enlarged blood vessels on the anterior surface of the iris follows, in point of time, the formation of peripheral adhesions in this type of primary glaucoma. Since these occur first in the upper, shal-

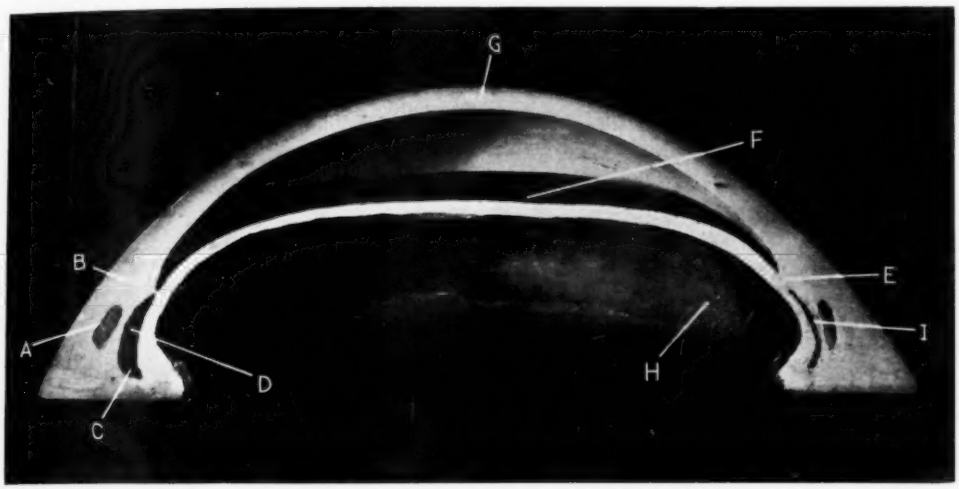

Fig. 4 (Otto Barkan). Model of shallow-chamber type of chronic glaucoma, showing peripheral adhesions forming. A, Schlemm's canal; B, closure of entrance to angle; C, sinus still open; D, sclerocorneal trabeculum; E, adhesion forming; F, anterior surface of iris; G, cornea; H, posterior surface of iris; I, angle almost obliterated.

under similar circumstances in cases of apposition of inflamed or congested surfaces in other parts of the body; as, for instance, peritoneum of the abdominal cavity or pleura. Such adhesions in the eye, it would appear, form as the result of aseptic inflammatory contacts or transudations associated with a local vasomotor crisis. These peripheral adhesions produce an additional and, this time, permanent mechanical block to the circulation of intraocular fluid. In addition, there is also some blocking of the flow of intraocular blood due to kinking of vessels in the iris. In this way the well-

lower part of the circumference of the angle the pupil is generally found drawn upwards.

Congestive symptoms may also occur in the late stage of deep-chamber or open-angle chronic simple glaucoma, though rarely, if the intraocular pressure rises rapidly enough as the result of a vascular crisis. This may occur in the terminal stage of this type, more especially in old patients who show marked vascular degeneration and instability. In these cases the anterior chamber retains its normal depth in contradistinction to those of the shallow type, and the angle remains open.

This fact, combined with the clinically asymptomatic history of the early stages, should prevent confusion with a congestive episode in shallow-chamber glaucoma.

Whereas congestive signs are the exception in deep-chamber glaucoma and occur only in its late stages, and then even rarely, they are characteristic of the early stages and are always present at some stage in the course of the shallow-chamber type. In the latter the entrance to the filtration angle is very susceptible to rapid and transient obstruction because of its narrowness. In the deep-chamber type, since the angle is open and the rate of blockage is extremely slow, congestive symptoms are practically absent until, as already stated, the final stage of "decompensation" has been ushered in. Evidently, when congestive symptoms do occur in this type of primary glaucoma they can hardly be due to increased rate of obstruction of outlet or to a suddenly increased retention of intraocular fluid. They must, rather, be the result of a too rapid change in the reflex vasomotor factor. This vasomotor change increases the intraocular pressure either by increased formation of intraocular fluid or by increasing the blood content in the uveal stream. This reflex would seem to represent a sudden attempt on the part of nature, analogous to a ureteral colic or vascular crisis in other abdominal viscera controlled by the sympathetic nervous system, to overcome the mechanical block.

From what has been said it seems more rational, especially from a surgical and therapeutic point of view, to classify the glaucomas anatomically and causally according to the above-mentioned anatomic pathogenic factors rather than, as has been done in the past, into "congestive" and "noncongestive" forms according to deceptive clinical behavior and appearance.

The deep- and shallow-chamber types of glaucoma described make up the vast majority of the primary glaucomas in the Americas and in Europe. In addition to these there are two other forms which should be included in a classification of primary glaucoma. One is the extremely rare form which is of purely neurogenic or vasomotor origin and the other is the glaucoma of epidemic dropsy in India. These forms will be discussed later.

Anatomic causal classification

The classification of glaucoma that one attempts will depend upon the point of view from which the subject is approached. The approach may be on a clinical or anatomic basis. For the purpose of surgical treatment the latter would appear to be the more practical approach.

In the past, primary glaucoma has been roughly classified into two clinical groups—inflammatory and noninflammatory, or congestive and noncongestive—according to whether or not inflammatory signs or congestive symptoms were clinically present. Heerfordt's[9] classification into lymphostatic and hemostatic glaucoma has the same underlying thought as has Elschnig's[10] classification into compensated and decompensated glaucoma. The latter terminology may, however, be misleading in its application to the eye and vision, since the word compensation in medical parlance suggests "functional equilibrium" (as in the case of heart disease). It is defined as "adjustment with absence of injury to the individual organ in question." In a case of so-called compensated glaucoma, however, when equilibrium has been established between the circulation of the intraocular fluid and the intraocular circulation of blood, this equilibrium is at an abnormally high level, and injures the optic nerve. As long as the nerve is subjected to this increased pressure it obviously cannot itself be in functional equilibrium, and its fibers,

which are subjected to this high level of pressure, must undergo atrophy as a result of it.

From a review of the literature, Raeder[11] and Curran[12] appear to be among the few investigators who have suggested an anatomic classification of the glaucomas in that they called attention to the varying depth and configuration of the anterior chamber. Raeder examined the position of the lens in glaucomatous conditions and stressed the dependence of the chamber depth upon the pressure in front of and behind the lens. His investigations showed that the static structure of the eye is such as to permit of different pressures in the anterior chamber and vitreous, but only when associated with a change in depth of the anterior chamber. Raeder suggested dividing the primary glaucomas into:

(1) Those with shallow anterior chambers in which the primary expansion originates in the posterior part. Peripheral adhesions may occur secondarily, as in acute inflammatory glaucoma and chronic glaucoma with or without inflammation.

(2) Those with normal or deep anterior chambers in which the primary expansion originates in the anterior part of the bulbus. To this latter type would belong infantile glaucoma or hydrophthalmus, juvenile glaucoma, and senile glaucoma simplex.

The results of my investigations confirm the wisdom of Raeder's suggestion. I believe that it is possible, and of great practical value, to correlate the anatomic causal types with the clinical picture, medical therapy, rational surgery, and general course of glaucoma. The causal classification may be summarized as follows:

(1) Deep anterior chamber, open angle; obstruction of the outlet is located in the pores or interspaces of the sclerocorneal trabeculum. This is that pathologic entity of gradually developing retention glaucoma which corresponds to and includes what has in the past been called "chronic simple glaucoma," "anterior glaucoma," "chronic noncongestive glaucoma," "glaucoma lenticulo-capsulare" (Vogt) and "glaucoma senile." It would seem that some forms of hydrophthalmos, juvenile glaucoma, and such secondary glaucomas as are due to stoppage of the pores of the trabeculum also belong anatomically, therapeutically, and surgically to this group. This type might aptly be called "trabecular glaucoma" in contrast to the shallow-chamber type, which might better be called "angle- or iris-block glaucoma." It can be only partially relieved by drops through the vascular or vasomotor mechanism; its rational surgery would seem to be "goniotomy" or any operation that incises the trabeculum, thereby reëstablishing outflow from the anterior chamber into Schlemm's canal. Where this is not possible a trephination or, in the writer's opinion, preferably cyclodialysis is in order. Because of the open angle and characteristic topography of neighboring parts, such as the ciliary body, trephination and cyclodialysis are attended by fewer complications in this deep-chamber type than in the shallow-chamber or narrow-angle type of glaucoma. Moreover, mydriatics may be applied with impunity postoperatively in this type, since the angle is open and the chamber deep, whereas in the shallow-chamber type mydriatics may cause adhesions in the angle postoperatively, and may even precipitate an acute attack of glaucoma, which I have seen to occur after a cyclodialysis operation.

(2) Shallow anterior chamber, narrow angle; the sclerocorneal trabeculum is permeable; transitory periods of increased intraocular pressure are due to temporary closure of the already narrow entrance to the angle. This is the entity that corresponds to what has been known as "chronic congestive glaucoma." In ad-

dition it includes many cases of shallow anterior chamber that have previously been erroneously regarded as chronic simple glaucoma because they had not yet begun to exhibit symptoms of congestion.

Predisposing anatomical or mechanical factors to a narrow entrance of the angle, may be a flat or small cornea (cornea plana, microcornea), flat limbal region, scars of limbus, hyperopia, increased size of the lens, or anterior displacement of the iris lens diaphragm of as yet unknown origin. Moreover, in my experience with three cases of glaucoma in retinitis pigmentosa, I am of the opinion that this condition also belongs in this anatomic group and is likewise relieved by the operative procedure to be described below.

It has been suggested that narrowing of the angle and shallowness of the anterior chamber may be due in many cases to a relative obstruction of passage of intraocular fluid through the pupil (increased physiological seclusion of the pupil). Operative results in iridotomy, as reported by Curran, as well as results of the procedure reported in this paper, offer strong evidence in favor of the presence of such an increased seclusion of the pupil.

In these eyes the entrance to the angle may easily become closed as the result of any factor that will displace the iris lens diaphragm anteriorly; for instance, sudden increase in the intraocular volume of blood, in the volume or pressure of the vitreous, or increased obstruction to the passage of the intraocular fluid through the pupil. Through anterior displacement of the diaphragm, contact between iris and the anterior surface of the lens is increased and thus a self-intensifying process would appear to be inaugurated. This tends progressively to increase the seclusion of the pupil and the anterior displacement of the diaphragm. Any one of these factors may precipitate a rapid closure of part, or the whole, of the circumference of the filtration angle, thus causing a rapid increase in intraocular pressure with consequent reflex vasomotor crisis, attack, transudate, and formation of adhesions. The events can be beautifully observed by the microgonioscopic method. These adhesions show no tendency to dissolve in time as do adhesions in the abdominal or synovial cavities. Thus the permanent peripheral adhesions of the iris of Weber and Kniess[13] are formed in the later stages of the shallow-chamber type of chronic glaucoma.

As the result of successive microgonioscopic examinations in the course of individual cases, it is possible to convince oneself that these adhesions are the result of the glaucomatous process and secondary to it rather than primary or causal. In this late stage with permanent peripheral organic adhesions, the eye is generally more or less resistant to treatment with miotics, depending upon the extent and location of the adhesions. Miotics rarely suffice to pull off any but fresh adhesions. Those rare cases, in which miotics reduce pressure in spite of apparent circular adhesions, usually show a small opening leading into the angle. Successful reduction of pressure through iridectomy in such a case suggests that only the entrance to the angle was closed and that the sinus behind it was open and permitted of filtration into the trabeculum. That the surgical treatment of the late stage of shallow-chamber type of glaucoma, when adhesions have formed, is beset with difficulties is not surprising when one compares it with analogous situations; for instance, in disease of the gall bladder or appendix with and without adhesions. The surgery of today in this stage of glaucoma is frequently inadequate and attended with undue hazards.

Surgical control

Need of adequate surgery for shallow-chamber type of glaucoma. There is great need for an operation which could be performed at an early stage, without hazard, before adhesions have formed, with the objective of preventing their formation and avoiding the development of this late stage.

Observers in the past concluded that the beneficial effect of iridectomy, either total or peripheral, or of iridotomy, was due to opening the angle of the anterior chamber and establishing free communication between aqueous behind and in front of the iris diaphragm. But in the absence of a method for adequate biomicroscopic observation of the angle before and after operation in one and the same case, such evidence necessarily remained presumptive. Furthermore, no definite choice of case was possible. With the improved microgonioscopic technique, it is possible by means of successive observations of the angle in one and the same individual to show and to correlate in point of time the various events and mechanical changes that accompany the development of increased intraocular pressure and its relief.

It can be shown that excision of the root of the iris, provided that postoperative adhesions in the angle are prevented, relieves increased intraocular pressure in the shallow-chamber type of glaucoma (quite irrespective of whether or not the eye is clinically congested). Since this is true it should be possible to define and to evaluate the mechanical disorder which is the cause of the increased pressure and to work out an adequate and safe surgical procedure for its relief and prevention. Such a procedure which is briefly described later in this article will be described in detail in another article.*

Iridectomy. Graefe's iridectomy was, from the beginning, almost uniformly successful in acute glaucoma. It was only moderately and occasionally successful in chronic congestive glaucoma. Its effectiveness in eyes successfully operated on can be shown to be due to the fact that both the acute and clinically chronic primary congestive forms of glaucoma belong to the shallow-chamber type where iridectomy is truly indicated, because of its action in affording access to the angle. It is understandable, in view of the classification suggested in this article, that when iridectomy was directed against other varieties of increased intraocular pressure (for instance, the deep-chamber and open-angle type) failures were usually recorded except where a filtering scar developed, or in those exceptional cases in which the incision happened to divide the trabeculum, thus creating a communication between Schlemm's canal and anterior chamber. It can be shown by means of microgonioscopy that iridectomy achieves no useful mechanical purpose in cases of the deep-chamber type, even when it is congestive, and does not reduce pressure unless temporarily following a paracentesis. It is useless and may even be harmful in this type unless an external fistulating scar accidentally forms. It is understandable in retrospect that ophthalmic surgeons of the past tried for this reason, among others, to evolve surgical procedures that might be substituted for iridectomy when this latter proved ineffective or dangerous, such as anterior sclerotomy, operation of de Vincentiis, combined sclerotomy of de Wecker or irido-sclerotomy of Panas. I believe it can be shown at this time that when these substitute procedures proved effective, their success was due to the incising of the blocked trabeculum and reëstablishing of communication between the anterior chamber and Schlemm's canal in deep-chamber cases only, never in shallow-

*Demonstration Session, Section of Ophthalmology, A.M.A., San Francisco, June, 1938.

chamber cases. Their frequent lack of success, even in deep-chamber cases, where they were mechanically indicated, appears to have been due to the fact that the surgeon operated blindly with his instruments hidden in the angle under cover of the opaque limbus.

In conclusion it seems evident at this time that iridectomy is for the shallow-chamber type of case and for this type only. But, even in these cases in which it is strictly indicated, classical, total, and peripheral iridectomy are often beset with difficulties and hazards that may interfere with successful results and may even endanger the eye. Indeed, in just this type of case the characteristic shallowness of the chamber renders it difficult to place the incision in such manner as to insure a truly basal location of the coloboma without endangering other parts, such as the anteriorly displaced ciliary body. Its too scleral placement results in dehiscence of the wound, delayed re-formation of the anterior chamber, incarceration of iris, or forward propulsion of the posterior contents, resulting in circular closure of the angle and a malignant course in high-tension cases. In the case of peripheral iridectomy, experience has shown that it is difficult and often impossible to obtain a basal excision of the root of the iris that is sufficiently large to be effective in permanently reducing increased intraocular pressure to normal. Peripheral iridectomy as practiced by Pflüger and Hess has, on the whole, proved inadequate even in the shallow-chamber type of case where iridectomy is indicated. Moreover, microgonioscopy shows that postoperative adhesions in the angle are frequent sequelae of iridectomy. These adhesions are so situated as to interfere with filtration and thus tend to nullify the effect of iridectomy or to aggravate the original condition.

Author's surgical procedure

As the result of these investigations it would seem that for a total iridectomy to be adequate in the shallow-chamber type of glaucoma, postoperative adhesions in the angle must be avoided; that for a peripheral iridectomy to be adequate and as effective as a total one in this type of glaucoma, its coloboma must extend over as much of the circumference as does the coloboma of the total iridectomy. This is extremely difficult to achieve and is often a physical impossibility. The same object can be achieved, however, by placing two or three peripheral iridectomies adjacent to one another, thereby covering a large part of the circumference and yet keeping the sphincter intact. Each excision must be basal and there must be no incarceration of the iris. Sometimes a single one correctly placed and executed is sufficient. To assure these conditions the following procedure is suggested:

It consists of preliminary deepening of the anterior chamber by means of injection of physiological saline solution.[14] Posterior sclerotomy facilitates the deepening in cases where the vitreous is liquid. In cases in which the vitreous is solid or there is high vitreous pressure and a very shallow chamber, in which a malignant course threatens, aspiration of 0.5 c.c. of vitreous with a syringe[15] may be employed. This appears to be clinically a justifiable procedure in this type of case and to be preferable to loss of nonfluid vitreous through a posterior-sclerotomy incision. Aspiration of vitreous is not necessary in those cases of the shallow-chamber type in which posterior sclerotomy suffices to soften the eye and to facilitate adequate deepening of the anterior chamber by injection. *This enables the mechanically perfect execution of one or several oblique valvelike keratome incisions placed within corneal tissue at the limbus.*

Through these, a corresponding number of portions of the root of the iris are excised. *The formation of adhesions within the angle is avoided since the chamber is deepened and the iris pushed back from the angle wall as the last step in the operation.* If aqueous is lost during the excision of iris the deepening can be repeated, which can also be done after completion of the operation in order not only to deepen the anterior chamber but also to avoid a too sudden reduction of pressure and to assure the achievement of the desired mechanical surgical result. Because of the oblique corneal incision combined with the deepening, the procedure avoids the dangers of delayed wound healing, formation of adhesions in the angle, intraocular hemorrhage from too sudden decrease of pressure, and malignant course.

The action of perforation of the iris diaphragm.—Any perforation of the iris partition in primary, chronic, shallow-chamber glaucoma which permits of free intercommunication between anterior and posterior chamber, results in a backward displacement of the iris that is most marked in the region of the perforation or aperture. This is clearly evident when the chamber is maintained as in the iridotomy of Curran and in the procedure to be described. If several such perforations are arranged next to one

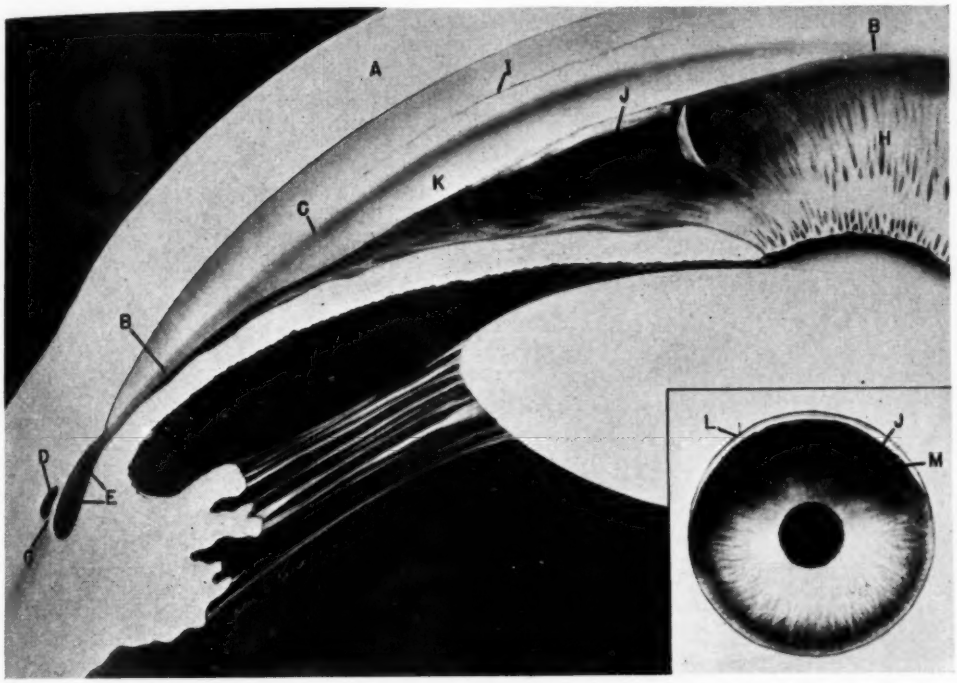

Fig. 5 (Otto Barkan). Shallow-chamber type of chronic glaucoma, showing result of operation. A, cornea; B, narrow slitlike entrance to angle; C, internal annular ring of Schwalbe; D, Schlemm's canal; E, sclerocorneal trabeculum; G, scleral spur; H, iris, anterior surface; I, keratome incision; J, excision of root of iris; K, deepening of chamber and widening of entrance to angle in region of operation.

Inset shows: J, multiple excisions of the root of iris; L, circumferential extent of widening of entrance to angle; M, upper shaded half of iris indicates deepening of chamber in this region.

another, the area of deepening in the anterior chamber is found to be correspondingly larger. As a result of this deepening, as shown by microgonioscopy, the entrance to the filtration angle becomes wider (fig. 5), an increased access of aqueous flow to the angle is produced, and there is less chance that mydriasis may cause blockage. Thus tension is normalized and congestive episodes are prevented in the future. Furthermore, it can be shown that perforation of the iris diaphragm is increasingly effective according to its proximity to the root of the iris. Excision of a small piece of iris halfway between pupil and limbus (semiperipheral iridectomy) or iridotomy has less effect on increased intraocular pressure than a peripheral iridectomy of the same size. The reason for this is that local action of iridectomy within the angle is brought into play in addition to the perforation of the iris and deepening of the chamber. The action of an iridectomy which extends to the root or base of the iris is well known:

(1) As described above, it causes retroplacement of the iris diaphragm, deepening of the anterior chamber, and widening of the entrance to the angle, thus affording increased access of aqueous to the angle.

(2) Access of aqueous to the trabeculum and undisturbed filtration is permanently assured in the region of the coloboma, since excission of the root of the iris makes its apposition to the wall of the angle impossible. In the case of iridotomy, on the other hand, or semiperipheral iridectomy, microgonioscopy reveals that the root of the iris does, under certain conditions, still come into apposition with and blocks the wall of the angle.

(3) At either extremity of the coloboma—that is, behind the root of each pillar—aqueous can enter the neighboring sinus of the angle and prevent the possibility of its complete circumferential blockage. A complete circumferential valve closure theoretically should not occur, since aqueous can still enter the sinus of the iridic angle by flowing behind the point of apposition of the iris at either end of the coloboma. Although the results of microgonioscopic investigation tend to confirm the older theories concerning the action of iridectomy in this latter regard, it is my impression that this does not by any means hold true in every instance. It is therefore advisable in many cases of iridectomy, even though tension has been normalized by operation, to continue with miotics in order to avoid a possible closure of other parts of the angle at some later date.

These observations can easily be confirmed by anyone who will measure the depth of the anterior chamber and examine the iridic angle with the binocular microgonioscopic method in the shallow-chamber type of case before and after operation. Even on the operating table and with the naked eye he will be able to repeat the observation, first made by Curran, of a funnel-shaped deepening of the anterior chamber around the site of iridotomy. I have found this to occur also when semiperipheral iridectomy is performed and in peripheral iridectomy when the anterior chamber is retained due to oblique corneal incision. I have, furthermore, seen a separate funnel form around each of the three adjacent excisions of the iris root, done at the same sitting. These funnels coalesced, thereby producing a general deepening of the upper half of the chamber during the course of the next few days. For this reason, multiple peripheral iridectomies or mutliple excisions of the iris root are more effective than a single excision.

In a few of these cases it was noted that the lower half of the chamber re-

mained shallow and that circular folds of iris stroma formed. These folds crowded the lower angle and gave the appearance as of slight forward prolapse of the lower half of the iris lens diaphragm, either absolute or relative to the upper deepened and straightened portion.

This widening of the upper part of the chamber angle, when combined with a basal excision of the iris tissue, appears to be sufficient to normalize intraocular pressure in the shallow-chamber type of case, and also to safeguard the eye against future episodes of intraocular pressure. It is fortunate that peripheral excisions of the iris tissue, covered by the upper lid, are not at all disfiguring nor obnoxious to the patient.

The glaucoma of epidemic dropsy in India and neurogenic glaucoma

In this paper it has been suggested that primary glaucoma is made up, in the main, of two major anatomic types, at least so far as the geographic regions of Europe and the Americas are concerned. Whether or not the glaucoma of India,[16] associated with epidemic dropsy and appearing to be causally related to a nutritional deficiency, comes under the heading of one of the above-described types or is of a completely different variety, it is impossible to state at this time. The anterior chamber of the glaucomatous eye in cases of epidemic dropsy has been described as having normal depth. This suggests a trabecular block as in the deep- or normal-chamber type of glaucoma mentioned in this article. However, in the absence of microgonioscopic examination, it is impossible to determine this fact. It may be that the increased intraocular pressure is due to physico-chemical changes in intraocular fluids.

Another type of primary glaucoma, and perhaps the only one which truly merits the term "primary," is extremely rare. It has been called "neurogenic" or "vasomotor glaucoma." In this type the anterior chamber is of normal depth and there are no anatomic anomalies detectable by means of any of the present-day methods, including microgonioscopy. There is likewise no constitutional disease present, unless it be a high degree of nervousness or nervous exhaustion. Indeed, this latter condition is characteristic and is probably the underlying cause of this type of glaucoma. It would appear to be a disturbance in the nerve control of intraocular pressure. Like other neuroses, it appears to be self-limited and does not require operative interference.

Postoperative use of miotics and the nature of surgical results in glaucoma

The conception that an operation for glaucoma in order to be successful should normalize tension without the use of drops is, in my opinion, not justified. It has been assumed that one should be able to dispense with drops after the operation and to dismiss the patient without the necessity of seeing him again, as in the case of appendectomy. That is, I believe, a false conception except for those patients who live in regions so remote that periodic ocular examination is impossible. The objective of operation in glaucoma is primarily preservation of function through control of pressure. In my opinion this can often be more successfully achieved by a judicious combination of rational surgery with occasional use of drops and periodic examination than by radical surgery, the aim of which is to dispense with the use of drops but which is attended by marked hazard and sequelae.

A good surgical result in glaucoma is preservation of visual function, and not necessarily reduction of pressure by operation alone without the use of drops.

Good results can be obtained by operation combined with the later use of drops with a much greater degree of safety and much less chance of later complications than by those operations which are intended to dispense with drops.

When one considers it dispassionately, the use of drops is not a major issue. In the shallow-chamber type of glaucoma adequate iridectomy or excisions of the iris root, performed according to the procedure described in this article, will keep the angle open in that region where the excisions have been performed. Since it is hardly feasible to perform multiple peripheral iridectomies throughout the whole cimcumference, it is only reasonable to keep the unoperated-on portion of the circumference of the angle open by means of drops. Furthermore, the continued pharamocologic action of miotics can only be of benefit. The opinion of ophthalmologists in the past has been that in order to obtain good surgical results in glaucoma it was necessary to dispense with drops. This was probably suggested by experience with iridectomy, which prevented the recurrence of attacks but did not always permanently normalize tension or prevent gradual deterioration of the visual function. In the light of microgonioscopic investigations this would seem to be due to two factors: (1) the frequent slight incarceration of a pillar or the formation of an adhesion in the angle postoperatively, and (2) closure of the angle later on in those parts of the circumference which had not been sufficiently influenced by the iridectomy. It would seem necessary, therefore, in order to achieve ultimate good results to (1) assure a technically perfect iridectomy without formation of peripheral adhesions and (2) to prevent gradual formation of adhesions in the angle outside the region of the iridectomy during the following years by keeping the root of the iris pulled out of the angle by means of drops, in the shallow-chamber type of glaucoma. It would appear that this result can be achieved by means of the procedure described in this article. Judging from the writer's experience in fifteen cases, it would seem that this technique, when combined with judicious use of drops postoperatively in those cases in which observation suggests there is need of them, will give ultimate good results. These results will compare favorably with those following more radical operations with preservation of the eye from any of their dangers.

Summary

On the basis of microgonioscopic and surgical investigations the main causes of increased intraocular pressure are becoming better understood. Glaucoma appears to be directly due, in the majority of cases, to mechanical obstruction of the circulation of intraocular fluid at some point along its course. These mechanical causal factors can be visualized in the living eye by means of microgonioscopy (biomicroscopy) and demonstrated by experimental methods. A classification of the glaucomas into major anatomic entities on a mechanical basis is suggested. In previous articles, primary glaucoma with a normal or deep chamber was described as an anatomic causal entity and a procedure (goniotomy) was suggested for its relief. In the present article the glaucoma with a shallow chamber is described and a surgical procedure is reported for its relief. The object of the procedure is to reduce increased intraocular pressure in a rational and safe manner by relieving the mechanical obstruction which is its cause and restoring the physiological direction of outflow of intraocular fluid. The procedure consists in performing one to several excisions of the root of the iris (multiple sublimbal or peripheral iridectomies) in

such manner that postoperative adhesions of the iris in the angle are prevented. The technique combines (1) deepening of the anterior chamber by means of physiological saline before, during, and at the end of the operation, (2) posterior sclerotomy and occasionally, in selected cases, aspiration of 0.5 c.c. of vitreous in order to facilitate the deepening of the anterior chamber, (3) performance of one or several successive oblique valvelike keratome incisions within corneal tissue near the limbus, (4) excision of one or several pieces of the root of the iris. Biomicroscopic examination shows the result of the procedure to be a posterior displacement of the diaphragm of the iris within the region of operation, deepening of the chamber with widening of the angle, and subsequent increased access of aqueous to the filtration angle. The effect is to reduce and prevent increased intraocular pressure in shallow-chamber (narrow-angle) type of glaucoma.

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Discussion

Dr. Frank E. Burch: I should like to ask Dr. Barkan if any untoward consequences of aspiration of the vitreous have occurred—any followed by hemorrhage.

Dr. Barkan: I have not observed any untoward consequences to date. There have been a total of fifteen cases, all of which, however, did not have vitreous aspirated. Some of them were posterior sclerotomies.

Dr. Frederick H. Verhoeff: The final test of the value of Dr. Barkan's procedures depends upon the results obtained. He says that his cases are yet so few that he cannot be sure of his results. Theoretical considerations as to the value of his operations are therefore in order.

First as to his operation of goniotomy. It seems to me if he actually cuts into the canal of Schlemm, this would ruin it, so that it wouldn't be good for anything at that particular place any more. He draws a picture indicating he has made a new open communication between the canal and the anterior chamber. If he gets this condition, he is getting something that is absolutely abnormal, because in a normal eye the canal of Schlemm does not open directly into the anterior chamber, but is separated from it by many spaces of Fontana walled off by endothelium, so that the fluid must go through several layers of endothelium before it can get into the canal of Schlemm.

If he can produce the condition he pictures, he is improving on nature to a great extent. That is not impossible, but I should guess that if he does get a beneficial result he does so by missing the canal of Schlemm, not by hitting it. Possibly he misses it often enough to accomplish something; that is, he permits the fluid to get in close enough connection with the uninjured canal to enter it.

This operation used to be done frequently many years ago, but not just as Dr. Barkan does it. I remember that Professor Haab on almost every operating day did what he called an anterior sclerotomy. He first performed a usual sclerotomy with a cataract knife, going through the limbus on each side, and then as he withdrew the knife he would sweep the point upward, and quickly cut into the filtration angle about half the way around. I couldn't tell how deeply he cut, and I don't suppose he knew, but his results must have been good because it was his favorite operation for chronic glaucoma. I should think that perhaps Dr. Barkan is simply doing the same thing, and I surmise that in neither operation is the canal of Schlemm cut into very extensively.

I suggested to Dr. Barkan that I would be better satisfied if he would take an eye that had been removed for some cause, such as a small sarcoma of the choroid, do his operation upon it, and then make a microscopic examination to ascertain what he had really done to the eye.

For his operation of deepening the anterior chamber, he gives Howard credit. Howard said the anterior chamber could be deepened to any desired extent simply by injecting fluid into it. I promptly wrote a letter to the American Journal of Ophthalmology, in which I denied this. I called

attention to the fact that I had been doing this operation for a good many years and had soon discovered that I couldn't deepen the anterior chamber to any great extent without rupturing the globe. The eye can hold only a certain amount of fluid, and it is already pretty full at the outset. The only way you can deepen the anterior chamber greatly is to let out fluid from the vitreous chamber before or at the same time fluid is injected into the anterior chamber. I never tried to remove vitreous, as Dr. Barkan does, but I made the incision just in front of the ora serrata. Very frequently there is no vitreous right there, and ordinarily you can get rid of a good deal of fluid without any loss of vitreous. If you do lose vitreous, this is a good place from which to lose it; it will do the least damage.

Dr. Barkan says he confirmed the observations of Curran, but he did not do what Curran did, which was to pass a knife into the anterior chamber and make a peripheral hole in the iris without evacuating the chamber. Dr. Barkan does an entirely different thing. He simply performs multiple small peripheral iridectomies. I have always been skeptical about Curran's theory of glaucoma, and in recent years I haven't heard any reports of anyone's doing his operation as a means of overcoming glaucoma.

I think it is possible that Dr. Barkan has hit upon two procedures that are very valuable, but I think it will take time to find this out, and in the meantime I am going to let him and other people find it out for me before I do either of the operations. (Laughter and applause.)

DR. J. N. OSBORNE: How wide is the incision in the cornea?

DR. W. M. BLACK: What was the tension of eyes, if tested, after removal of vitreous?

A THIRD QUESTION: The theory of the goniotomy is to increase the means of exit of aqueous through the normal channel. Is the theory of multiple iridectomy similar? Please illustrate how the iridectomy, as you do it, aids in evacuation of the aqueous.

DR. BARKAN: I am especially grateful to Dr. Verhoeff for his criticism, and would like to answer to the implied question.

I believe that in the goniotomy operation one cuts into the canal of Schlemm, because I tried on the enucleated eyes of a hanged man to locate the canal in its relationship to the gonioscopic appearance of the angle, by means of placing markers from the outside into the angle, and it turned out that in these two cases when they were examined microscopically later on, the markers had traversed Schlemm's canal and come out in the angle just anterior to the scleral spur, and that is a definite landmark in the gonioscopic appearance, and the pigment band is just anterior to the scleral spur.

That is rather a roundabout way of arriving at a conclusion, but I think it indicates that the incision, when it is just anterior to the scleral spur, is cutting into the canal, or maybe is tearing off some trabeculum and thereby causing a leak from the chamber into the canal, as Dr. Verhoeff suggests. In any case, those incisions which are not in this region (and they constitute about half of the incisions I have made to date, I believe) have not reduced the pressure.

Goniotomy I have performed in eleven cases, which cover a period of from one to two years—no, I should say it has reduced the pressure to normal in eleven cases, the durations of which are from one to two years. Some of them have to use drops. I believe, and I am glad that Dr. Verhoeff brought it up, that the anterior sclerotomy that Haab and many of the European ophthalmologists used, creating a division between these—

de Wecker's internal sclerotomy, for instance—was based on that theory, and I have always been struck by the fact that so many Continental operators have continued to use anterior sclerotomy.

I have seen two cases gonioscopically which had been normalized. They had been operated on elsewhere for a period of several years, and in these the incision was just at the edge of the trabeculum, and I surmised they had been normalized. Apparently they closed up and needed renewed operation; on one I performed a goniotomy, and that one is normal today —after a period of over a year, certainly.

I have not had occasion to operate on an eye with normal anterior chamber such as Dr. Verhoeff suggests. I have been watching for one and hoping for one.

Scalinci used de Vincentiis's original method of incising the iridic angle. I did this in two cases and made microscopic sections of them later on. I cannot tell you just as this moment—it has slipped my memory—whether they showed a communication between Schlemm's canal and the anterior chamber. I believe they did.

In regard to the aspiration of vitreous, I am very much interested to receive the suggestion from Dr. Verhoeff of making an incision near the ora serrata. I have never tried that, and perhaps I am as timid in trying it as he is in trying an aspiration.

The peripheral iridectomy that I have performed is perhaps not completely analogous to Curran's iridotomy, but there are many similar features, because in some of these cases the anterior chamber was retained, and I did not have to deepen it. It is true that the iris had to be pulled out and that, no doubt, caused some effect upon it, but in Curran's iridotomy there is some pulling and extension of the iris, too.

In answer to Dr. Osborne, how wide the incision is in the cornea, I gather he refers to the incision with the keratome in the second procedure. Am I correct?

DR. OSBORNE: Yes, sir.

DR. BARKAN: I haven't measured it. I suppose it would be three to four millimeters externally. It should be just so large that the internal-wound lip permits an opening of iris forceps a little. There are bridges between these separate incisions and that is why I believe there is no possibility for postoperative astigmatism.

Dr. Black asked what the tension of the eyes was before aspiration of vitreous. Am I correct in that?

DR. BLACK: After aspiration of vitreous.

DR. BARKAN: Judging by the dimpling with implements, they were softening; in fact, I should think they were softening quite a little because I had the feeling that it was well to inject the chamber in order to restore the pressure, to prevent intraocular hemorrhage, which might be possible.

As to the third question: The theory of goniotomy is to increase means of exit of aqueous material in a normal direction. The channel, after incision or removal of the trabeculum is, of course, abnormal.

I used the expression "normal direction" in contradistinction to the other operations which create an abnormal direction of outflow, such as trephining, iridencleisis, and cyclodialysis. In a general way the theory of multiple iridectomy is similar because it permits of the outflow of aqueous through the filtration angle, through the trabeculum into Schlemm's canal, rather than creating an abnormal direction of outflow, as is the case in the external filtering operations.

I should like to add that it is not always necessary to make multiple iridectomies. One may be sufficient provided that adhesions are prevented.

DR. HORNER: Do you consider your

keratome peripheral iridectomy through the cornea better than *ab externo?*

DR. BARKAN: I am particularly glad that Dr. Horner asked this question because, after having performed several operations with the method described, I felt it would be advisable it if could be done, to avoid both posterior sclerotomy or aspiration of vitreous, or deepening of the chamber, and in order to avoid the possible dangers inherent in these procedures, I tried five cases by the *ab externo* method. I did multiple iridectomies *ab externo* and found it, of course, very convenient to reach the root of the iris.

I endeavored to make the incisions as oblique as possible in order to obtain the value of action which would insure quick restoration or maintenance of the anterior chamber, but in spite of that, found there was a certain delay of two or three days, let us say, of complete restoration of the chamber.

Now, those cases, when examined microgonioscopically later on, showed a tendency to peripheral adhesions. One of them that I happened to look at last night, and which is highly successful, showed anterior adhesions to the inner wound but not peripheral adhesions. Between the anterior adhesions one sees there has been a posterior resection of the iris and an opening of the angle above, with normalization of pressure, without the use of drops in this case, but in some of the others of these five, pressure returned, or the constant use of drops was necessary, and I believe that was due to the delayed closure of only a few days, which is consequent upon the *ab externo* incision, and it is for this reason that I think in the future I will continue with the other method and not this one; that is, with the other approach and not the *ab externo* in this particular procedure.

DR. FREDERICK H. VERHOEFF: I should like to ask Dr. Barkan another question: How deep do you make the anterior chamber and how much pressure do you think you get in it before you make your incision? Assuming, as I think he will tell us, that he makes the anterior chamber considerably deeper than it was, will he say whether this alone would not pull off the adhesions and free the filtration angle?

DR. BARKAN: I deepened the chamber considerably. I believe this has been described by Howard. One actually pushes the periphery of the lens backwards, so that the posterior chamber is abolished, and the pupils dilate somewhat. In the cases with posterior sclerotomy and a solid or semisolid vitreous, it was necessary to raise the pressure a great deal, almost obtaining a semicornea, in order to deepen the chamber, and that is why in those cases I have gone on to aspirating a little vitreous.

As I went on to excise the pieces of iris, I don't know what the ultimate effect of a deepening or aspiration of vitreous, either, alone or together, would have been. I do not think that it would have had any permanent effect because, even following upon the multiple iridectomies, the chamber shallows again in the course of the next two weeks. It does remain a little deeper, about, in the operated region, two or three tenths of a millimeter, but the lower part is anteriorly displaced again to about the position where it was before.

I wish to thank the members of the Society for their interest and questions and discussion.

KAYSER-FLEISCHER RING—WILSON'S DISEASE*

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Three case of hepatolenticular sclerosis, with the Kayser-Fleischer ring, are here reported. The first two cases occurred in a brother and sister and present the usual picture of consanguinity, heredity, corneal ring, and neurological symptoms. The third case is representative of the so-called atypical class.

Case 1. R. E., a white male, aged 22 years, was admitted to the Johns Hopkins Hospital on January 1, 1935. The complaint was difficulty in speech, tremor of the hands, and also difficulty in walking.

The great grandparents were cousins. There were two daughters from this union, who married two brothers. One of the resulting families was healthy, with the exception of one child who died after a long illness complicated by neurological symptoms. The second family consisted of ten children, two of whom died in infancy. The other eight children, one of whom is the father of the first two patients here described, were healthy.

The immediate family to which the first two patients belong consisted of ten children. Two brothers and one sister died at the ages of 15, 18, and 22 years, respectively, after long illnesses. From the description, these illnesses appear to have been hepatolenticular sclerosis. Four sisters and three brothers were healthy, although two of them had children with neurological disorders, one dying in infancy.

The patient had whooping cough, scarlet fever, and chickenpox, and two attacks of jaundice as a small child, otherwise he had been healthy up to the onset of the present illness.

This began at 14 years of age with a fever of three weeks' duration which was thought to be paratyphoid. Toward the end of this illness a thickness and heaviness of speech developed, associated with difficulty in pronunciation. Speech became rapid and unintelligible, but was strongly controlled. Except for this speech difficulty there were no symptoms for some years, up to November, 1933, when the patient was 20 years of age. He then suffered a dislocation of the jaws, which subsequently recurred frequently. At about this time he developed a right-sided earache without discharge; and an ulcer developed on the right shin, which healed slowly. After two or three months he noted a tremor of his left hand. The tremor soon coarsened, lengthened its excursion, and spread to involve the arm, the head, the right hand and arm, and finally the upper trunk. The tremor was rhythmic, was absent in sleep, but increased on purposeful effort or excitement. Although it did not involve the legs, the gait gradually became more unsteady, and he occasionally fell. He developed a fixed smile and twitching and jerking of the facial muscles. His appetite gradually increased and this was paralleled by increasing constipation, painful defecation, urinary incontinence, and strangury. He had done light work on the farm immediately before he presented himself for examination.

Physical examination showed a well-developed man of 22 years. The mouth was held open most of the time, and occasionally saliva drooled from it. The general facial expression suggested stu-

* From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. Read before the Ophthalmological Section of the Baltimore City Medical Society, 1937.

pidity, although the patient was alert and coöperative. The head was bent forward, and there was a slight flexion of the upper part of the trunk. He spoke in a monotone, with poor enunciation, the lips and tongue moving only slightly. Replies to questions were usually accurate and definite. The patient was well oriented, did simple arithmetic correctly, and answered simple questions on current events. He was abnormally cheerful and grinned as he told of his brother's death from an illness similar to his own.

The cranial nerves one, two, three, four, six, and eight were normal. The frequent dislocation of the jaw suggested involvement of the fifth nerve, but the jaw muscles were firm although smaller than usual. The expressionless appearance of his face and the drooling suggested involvement of the seventh nerve, but the face and the mouth could be moved voluntarily as directed. Slight movement of the palate on phonation, difficulty in swallowing fluids rapidly, and indistinct phonation pointed to possible involvement of the ninth, tenth, and eleventh nerves. The tongue was small, but not atrophied. Hence the twelfth nerve probably was not affected.

The musculature was well developed and firm. The head was bent forward slightly with the upper part of the trunk. There was no flexion of the legs. The arms were held in abduction at the shoulders and there was questionable slight internal rotation. The fingers were almost completely extended and abducted in a manner suggestive of the posture of athetosis. When the patient was seated there were no involuntary movements. When the arms were outstretched, coarse, irregular oscillations appeared and shook the trunk slightly. If one arm was stretched out and the other arm supported, a fairly rhythmical tremor of moderate amplitude appeared in the supported arm. This tremor closely resembled the Parkinsonian type. On passive movement there was some rigidity in the arms and legs and at times a suggestion of cog, but this was neither constant nor typical. At other times there was scarcely any rigidity. Strength was good in all muscle groups. The finger-nose test brought out a coarse, violent tremor which involved not only the arms but the head and trunk and resembled the intention tremor of the cerebellar syndrome. Finger movements were slow and stiff, so that the patient could not fasten buttons. The heel-knee test was well performed. The station was fairly steady when the eyes were held open, but at times the patient swayed and fell backwards. The gait showed little change. The base was broadened and the legs advanced somewhat stiffly.

No loss of sensibility was discovered. The tendon reflexes were all readily elicited. The knee jerks were rather brisk, and a few jerks were elicited on attempting to obtain ankle clonus. The abdominal reflexes were present and equal. The plantar reflex was equivocal, but a downward movement was obtained oftener than an extension.

Examination of the abdomen revealed absence of liver dullness in the midclavicular line. In the anterior axillary line the dullness measured 7 cm. from the fifth to the seventh interspace, and in the midaxillary line it measured 6 cm. from the sixth to the seventh interspace. The spleen could not be palpated, but the area of splenic dullness was slightly increased.

Ophthalmological examination revealed absence of ptosis, nystagmus, and exophthalmos. Vision was 20/15 O.U. On close inspection a greenish-yellow pigment ring was seen to encircle the cornea just within the corneoscleral margin. It was uniform and approximately 2.5 mm. wide. The cornea was otherwise clear.

The anterior chambers, irides, pupils, external ocular movements, pupillary reaction to light and accommodation, and tension to fingers were normal. Ophthalmoscopic examination revealed normal nerve heads and fundi. Slitlamp examination showed the greenish-yellow color and the granular or stippled appearance to be confined to Descemet's membrane at its periphery, occupying a band 2.5 mm. wide. The color and stippling were more pronounced at the periphery of the band. No other abnormality was detected. Both eyes were similar in appearance. Visual fields seemed normal on rough test.

The usual laboratory tests were performed and were not remarkable. These included urine tests, blood counts, and gastric analysis. Examination of the cerebrospinal fluid showed one cell, a negative Pandy, and 25 mg. percent protein. Wassermann tests on the blood and spinal fluid were negative. Special tests were also performed. X-ray examination of the head and abdomen were negative, as were the Van den Bergh and bromsulphthalein tests. The bilirubin liver function test showed 25 percent retention after four hours. The patient was discharged on January 12, 1935, without treatment. He was cared for elsewhere and died in the late summer of 1935.

Case 2. D. E., a white female, aged 13 years, was admitted to the Harriet Lane Home of the Johns Hopkins Hospital on January 1, 1935, complaining of thickened speech, stiffness of fingers, and increased flow of saliva.

The patient was a sister of R. E. (case 1). She had had no diseases except mumps several years previous to admission, and had apparently been normal until two months before admission, when it was noticed that her speech was becoming a little thick, and that her fingers seemed stiff at times. There was increased salivation.

Physical examination. The face was masklike, with open mouth. Her posture was not constantly altered but there was at times some flexion of the elbows and possibly slight flexion of the head. There was little rigidity at the elbows and no outspoken tremor, but when she was writing a fine oscillation of the head and of the other hand appeared. Writing was slow and labored, and the script irregular, though quite legible. Speech was slow and labored, but quite intelligible. The gait was normal.

No sensory changes were detected. Tendon reflexes were not abnormal. Examination of the abdomen revealed no abnormality. The lower edge of the liver could just be felt. Liver dullness was not increased.

Examination of the eyes disclosed a Kayser-Fleischer ring similar to, but not so well developed as in her brother, in that the ring was slightly narrower. With this exception no ocular pathology was discovered. The patient was discharged January 12, 1935, unimproved. Since then she has disappeared from observation.*

Case 3. L. G., a white female, aged 38 years, was admitted to the Johns Hopkins Hospital in February, 1926, complaining of reduced vision.

Both mother and father had had diabetes. One brother subsequently developed pulmonary tuberculosis. No history of consanguinity or neurological disease in the family could be elicited.

The patient had had cervical adenitis in early childhood; tonsillitis and tonsillectomy at the age of 14 years; acute rheumatic fever at 22. Her past history was otherwise unimportant. She had had no

* Cases 1 and 2 were studied by Dr. F. B. Walsh, through whose courtesy they are here presented.

trouble with her eyes until the onset of her present illness.

This began in 1925, when the patient came to the Ophthalmological Out-Patient Department complaining of congestion of the eyes, headaches, and poor vision. Examination at that time showed a slight anisocoria; sluggish pupils; a scar in the lower portion of the left cornea; a small degree of compound hyperopic astigmatism in the right eye, which was corrected to 20/30, and vision of 2/100, unimproved, in the left eye, due to an old iritis.

Later the patient developed recurrent episodes of numbness of the hands and face, with slight motor disturbances, and came to the Neurological Out-Patient Department. Examination at that time showed some irregular tremors and slight disturbances of coördination. There were insufficient data to permit a diagnosis, but the possibility of multiple sclerosis was considered. Examination of the eyes at this time showed evidences of a recent iritis in the left eye, with posterior synechiae and old P.K. deposits. The corrected vision at this time was, R.E. 20/30—, L.E. 20/200. There was a moderate degree of tuberculin sensitivity (1/100 mg.), and tuberculin was given from 1926 to 1930, up to 70 mg. There was no improvement under tuberculin therapy, and in 1929 a sharp painful attack of uveitis occurred in the right eye, with failure of vision. During November and December of 1931 there was a further sharp loss of vision in both eyes and periods of diplopia. There was no history of iridescent vision. Synchronous with the development of this visual failure, further neurological symptoms developed. These were manifested by a dragging sensation in the right leg and unsteadiness of gait. Objectively the patient developed a positive Romberg sign, loss of vibratory sense, and of passive movement of the legs, with increased knee and ankle jerks, and bilateral extensor responses. On January 4, 1932, the patient was admitted to the Wilmer Institute.

Physical examination. The general physical examination was negative except for the ocular and neurological findings. The laboratory studies were all negative. Blood chemistry was normal, hemocytology was normal, the Wassermann reaction negative, the blood pressure normal, the urine negative, and the renal function normal.

Examination of the eyes showed an acute secondary glaucoma of the right eye, with hazy cornea, iris bombé, posterior synechiae, and media so cloudy that the fundus could not be seen. Vision was reduced to 2/100 and the tension was 60 mm. Hg. The left eye was quiet, with evidences of old iritis; vision was reduced to 15/100, and the intraocular tension was 25 mm. Hg. Ophthalmoscopic examination was unsatisfactory owing to the contracted pupil. The slitlamp examination of the corneae showed a generally dull, hazy cornea in the right eye. In the left eye the cornea was clear, except in the lower quadrants where the general appearance suggested a dystrophy.

A peripheral iridectomy in the right eye was followed by a drop in tension and subjective relief, but with no improvement in vision.

The neurological examination at this time was as follows:

Cranial Nerves.

I. Intact.
II. See history.
III, IV, VI. No ptosis, squint, diplopia, nor nystagmus. Ocular movements of full range.
V. No numbness in face, nor pain in the fifth-nerve distribution. Sensibility is intact. Corneal reflexes equal. Jaw muscles act well and there is no deviation.
VII. Face is symmetrical at rest, and volun-

tary and emotional movements are equal.

VIII. No subjective disturbances of hearing. Hearing is within normal range as tested with watch and tuning fork. No aural vertigo.

IX, X, XI. No weakness of the soft palate no disturbance of phonation nor of swallowing. Pharyngeal reflex present. No weakness nor atrophy of sternomastoids or of trapezii.

XII. Tongue protruded in midline without tremor or atrophy.

Motor system. Posture not abnormal, but patient holds head slightly flexed. No muscular atrophy. On passive movement there is pronounced spasticity of the right leg and slight spasticity of the left. The fingers of the right hand are slightly slow and clumsy as compared to those of the left. The patient is right handed. Heel-knee test shows clumsiness of the right leg and definite ataxia of the left leg. The gait shows loss of equilibrium and ataxia in the left leg. The left foot is everted. The speech is clear.

Sensory system. No pain nor numbness. Cotton wool, pin prick, warm and cool are well appreciated over the body and extremities. The sense of passive movement in fingers and toes is intact. Vibrations of the tuning fork are well appreciated. No astereognosis. No tenderness of skull, bones, muscles, or nerves.

Reflexes. All the tendon reflexes are very active. The right knee jerk is greater than the left. No clonus. Abdominals: right, absent; left, feeble. Right plantar extensor; left, equivocal.

A diagnosis of multiple sclerosis or pseudo-sclerosis was made. The patient was discharged from the Wilmer Institute on January 12, 1932. She was readmitted on June 20, 1932, with a diagnosis of bilateral acute glaucoma. A cyclodialysis was performed on the right eye, and a corneoscleral trephining on the left. At her discharge, on June 30, 1932, the vision in the right eye was 20/100 and in the left eye 20/70.

On this admission it was noted that there was a definite dystrophy of both corneae, with a greenish hue in the lower and deeper layers. The neurological examination was essentially unchanged. Because of the corneal dystrophy with the greenish discoloration of the lower quadrant of the cornea, especially in the deeper layers, and the atypical neurological symptoms, it was thought the underlying condition might be an atypical form of Wilson's disease.

After discharge from the hospital the patient's course was steadily downwards. A vaccine prepared by the Purvis-Stewart method from the spinal fluid was given intravenously without bringing about any improvement. Vision continued to fail and on January 4, 1936, the patient was completely blind. She was last seen on June 6, 1936, at which time she could not walk without an attendant, due to the weakness and incoördination of her legs.

Comment

In a review of the literature of Wilson's disease, it is quite clear that there is a lack of uniformity on the criteria for diagnosis. One group of authors limits the diagnosis of hepatolenticular sclerosis to those patients showing the typical corneal ring and classical neurological findings. Others believe it to be a large general-symptom complex, dependent more on constitutional factors than on heredity, and include in the category of Wilson's disease a large number of patients with the general picture of pseudosclerosis and indefinite ocular symptoms.

In the earlier investigations three main lines converge regarding the conception of hepatolenticular degeneration: first, studies of the connection between nervous and hepatic lesions; second, the clinical and pathological differentiation of pseudosclerosis as a nervous disease; and, third, the corneal ring. Recent researches consider a mineral metabolism and the conception of the disease as an abiotrophy.

Strümpell[1] in 1878 reported a case resembling multiple sclerosis and Westphal[2] in 1883 gave it the name of pseudo-

sclerosis. Studies by Kayser[3] and later by Fleischer[4, 5, 6, 7] advanced the knowledge of the symptom complex. The neurological and ophthalmological lines here converge.

Wilson[8] in 1912 described the disease as an affection of the extrapyramidal system.

Hösslein and Alzheimer[9] discovered the definite microscopic lesion in the brain. Alzheimer gave extensive descriptions and presented beautiful drawings of the giant glia. He did not mention the corneal ring. In this case the onset began at 15 years of age and the duration was seven years.

Hall of Denmark[10] collected 68 cases. He brought together pseudosclerosis, torsion, spasm, and Wilson's progressive lenticular degeneration into a single morbid entity and proposed the name of hepatolenticular degeneration. Lüthy[11] discussed particularly the trends in the study of the disease since Hall's publication. Among the most interesting of these are the geographic distribution of the disease, the metallic metabolism, the genetic relationships, and the conception of the disease as an abiotrophy.

In 1888 corneal pigmentation was described in Eichhorst's clinic. The first published case was by Kayser, who did not, however, relate the pigment ring and the nervous symptoms. Salus[12] was apparently the first to recognize the connection of the ring with the nervous disease. Fleischer, in 1910, brought out the clinical determination of a new syndrome based on the further clinical study and autopsy findings. The syndrome consisted of corneal pigmentation, generalized pigmentation, hypertrophic cirrhosis, glycosuria, and nervous symptoms resembling pseudosclerosis. He showed that the nervous disease was not multiple sclerosis.

In Hall's review of 68 cases, the ring was found in 21, of which 16 were of the pseudosclerotic type, 4 of the Wilson type, and 1 doubtful.

Siemerling and Oloff[13, 14] reported pseudocataract, in addition to a corneal ring, in hepatolenticular degeneration.

Corneal ring has been observed in a few conditions other than hepatolenticular degeneration. Holzer[15] was the first to report it as a part of a transient lenticular syndrome following epidemic encephalitis. Jess[16] in 1922 reported four cases of copper impregnation of the cornea similar in appearance to the Kayser-Fleischer ring. Wimmer[17] of Copenhagen gave a clinical and pathological report of a case of extrapyramidal disease with corneal pigmentation but without hepatic lesions. Günther[18] observed "traces" of a bilateral corneal ring in a case of hemichorea accompanying advanced chronic nephritis.

Pelnar[19] gave the clinical and gross pathological report of a case of hepatolenticular degeneration in which corneal pigmentation, present in 1920, had disappeared in 1922, except for a trace scarcely visible at the time of death. He concluded that the ring may be present in only one phase of the disease and that a single negative report is inconclusive.

The nature of the pigment has given rise to a prolonged controversy, with confused and conflicting evidence, and it is still an unsettled question. Fleischer was the first to study its microchemical reactions. He found that it did not give reactions for iron and that it was resistant to the most varied reagents—alcohol, ether, chloroform, acid, and alkalis—but was soluble in ammonium sulphide. Later investigators have, in general, confirmed these findings. Fleischer considered it improbable that the pigment was of biliary origin because it is insoluble in alkalis and does not give the nitric-acid reaction. He thought, nevertheless, that it was probably some unknown degenera-

tive product of the blood. In 1913 Rumpel[20] suggested that it was silver. He based his opinion on the examination of the formalin-fixed liver and kidneys in Fleischer's first case. It is not stated in his article that the eyes, brain, and meningies were examined. The chief protagonist of the silver theory in recent years has been Vogt.[21, 22] His evidence rested first on the identity of the slitlamp pictures in patients treated for corneal ulcers with silver preparations and in cases of pseudosclerosis with corneal ring; and, second, in the solubility of the ring pigment in potassium cyanide. Only silver and gold are soluble in this reagent and not organic pigments. In his latest communication,[23] however, Vogt expressed himself as doubting whether the ring pigment is always of the same nature because it does not always behave the same way in colloidin and paraffin sections and may vanish in the latter. Again, pseudosclerotic patients do not always store up the same metals. Copper is one of the most commonly accumulated, and copper cataract is a sign of auto-intoxication from excess of the metal. In Vogt's opinion there are two groups of cases showing pigmentation of Descemet's membrane; namely, those with silver, probably including also the cases which Strümpell mentions as an argyrosis, and those not containing silver.

Kubik[24, 25] was the first to study with the microspectroscope the ring pigment in two living eyes. He found that the spectrum was very similar to that of urobilin. Hessberg[26] also examined with the microspectroscope a case of pseudosclerosis showing a pigment ring in the cornea in one eye; in the other, a pigment ring on the free edge of the lens was rendered visible by a congenital coloboma of the iris. Both rings gave a definite urobilin spectrum. Kubik believes it safe to assume that the pigment is endogenous and that it reaches Descemet's membrane by way of the aqueous. He reported an exhaustive microchemical study of the eyeballs from two cases of Wilson's disease in frozen sections and colloidin embedding. His conclusions are that urobilin and hemosiderin can be excluded; likewise silver, iron, and copper.

Among the known pigments, the ring resembles most the autochthonous pigments found in the ganglion cells and the myocardium in cases of brain atrophy; probably an organic compound related to the lipoids and of a complex structure. The composition of autochthonous pigments differs widely in the same individual, according to the site of origin. Although not isolated, it appears that they are composed of a fat and pigment body, combined loosely and in variable proportions. Kubik's impression was that the pigment is a product of the endothelium, probably somewhat of the same nature as in an arcus senilis.

The most recent contributions are those of Gerlach and Rohrschneider[27] and of Fleischer and Gerlach.[28] Their researches involved the application of the new and extremely sensitive spectroscopic method of the high-frequency spark, and they concluded that the pigment does not consist of silver. The eye showed a trace of copper, which was considered physiological. In another case the corneal ring, lens, and vitreous were studied. In the corneal ring the presence of copper was greater than in the other structures and there was also present a trace of iron.

A critical discussion of the process of deposition of metals, particularly silver and copper, in the cornea is given by Sollmann.[29]

A number of observations have been made on the increase of copper in the body in cases of hepatolenticular degeneration with corneal ring. The finding of a copper pseudocataract has already

been mentioned. Vogt found a great increase of copper in the liver, kidneys, and spleen; Kubik and Fleischer and Gerlach in the liver and spleen; and Haurowitz[30] in the liver and basal ganglia.

The increase of copper in the liver is by no means confined to hepatolenticular degeneration but is present also in other forms of cirrhosis. Whether it has an etiological relationship to either the hepatic or brain lesions is unknown. The exact site of the pigment and the factors determining its localization have been discussed by Jess, Kubik, and Sollmann, also by Weger and Natanson.[31]

The metallic metabolism in the hepatolenticular degeneration has been discussed. Lüthy found a pigmentation of the skin in 16 patients, 14 of whom had a corneal ring. He considered the pseudocataracts to be quite evidently signs of disturbed metallic metabolism. In pseudosclerotic brains analyzed for copper, the content was found to be approximately 10 times the normal.

Fleischer stated that the corneal pigmentation is only part of a very characteristic pigmentation involving parts of the body, particularly the sclerotic connective-tissue membranes. He reported two cases which came to autopsy and showed hypertrophic cirrhosis of the liver and a light-brown discoloration of the internal organs, due to deposition in the connective tissues of a finely granular, brownish pigment.

Lüthy remarked that the geographical distribution of hepatolenticular degeneration has been little studied. Of his 120 cases (without regard to corneal ring), 52 were from Germany, 3 each from France and Italy, and 1 each from Spain and South America. There was only one doubtful case of corneal ring in a French person, although a number of cases from other countries have been published in French annals. In the accessible Italian reports the ring is not mentioned. Rodriguez-Arrias, Cortes-Llado, and Perpina-Robust[32] felt sure that their case was the first one with corneal ring to be reported in Spain.

The author has been able to collect 89 additional cases of corneal ring in hepatolenticular degeneration from the literature. In addition, three doubtful cases were found. A number of other reports were not accessible. The geographic distribution of these 89 cases is as follows:

Germany	47
United States	11
Czecho-Slovakia	7
Switzerland	5
Russia	4
Denmark	4
Sweden	3
England	2
Holland	2
Esthonia	1
Spain	1
Poland	1
China	1
Canada	1

Of these cases five followed epidemic encephalitis. There were four cases of corneal ring in connection with copper cataract, and one case of corneal ring in connection with hemichorea.

Curschmann[33] summed up the general picture as follows: "The conception of a hepatolenticular degeneration or Wilson's disease and pseudosclerosis is that they are the end results of constitutional and not of exogenous factors; that the two conditions, although similar, are not identical. They form a chain of pathological conditions, at the end of which are those benign, extremely chronic forms, appearing rather as an anomaly of morbility than as a disease; and, at the other end, the acute lethal cases of Wilson's disease and the quickly dementing cases of the original Westphal-Strümpell type, ending in epileptoid seizure and complete contracture."

In his discussion of Wilson's disease, K. Loeoy[34] gives the following summary.

"The Wilson sclerosis group is better adapted to solving the problem. Nevertheless, analysis of cases fails to show a chronological relationship between the hepatic and striate affections. The two do not stand in causal relationship, but the familial occurrence and recessive inheritance show that the four chief symptoms of the Wilson pseudosclerosis group (spongy degeneration, characteristic of the Wilson type; glial proliferation with Alzheimer cells, characteristic of pseudosclerosis; the peculiar cirrhosis; and the corneal ring) can occur in the most varied combinations of the genes. The disease is bound up with different linked hereditary factors, which determine the vulnerability of liver and brain. It occurs in families afflicted with hereditary nervous disease and alternates with other nervous and liver diseases."

As to the pathogenesis, in Wilson's opinion the disease is acquired and not due to congenital defect. There is nothing essentially familial about it in spite of the frequent occurrence of several cases in the same family. He believed the syndrome to be due to a toxin, possibly absorbed in the liver.

The features of the disease fit in best with the assumption of a toxic agent. As the disease is probably hereditary, the conclusion by analogy would be that it is based on a primary disturbance of metabolism.

In the literature of case reports the ages varied from 10 years, the youngest, to 68 years, the oldest. The duration of the disease was from 1 month to 43 years. The atypical cases form the largest group.

Hepatolenticular degeneration

Evolution of the Conception

Frerichs, 1858, was the first to study the relationship between the liver and the nervous system. The first recognition of hepatolenticular degeneration possibly goes back to his description in his Klinik d. Leberkrankheiten (1861) of a case with peculiar nervous symptoms and severe changes in the liver.

Strümpell, 1878, reported a case resembling multiple sclerosis in which he found abnormal hardness of the brain.

C. Westphal, 1883, reported two similar cases. As he found no gross changes in the brain he considered the disease to be a neurosis, and because of its resemblance to multiple sclerosis, called it pseudosclerosis.

Between 1888 and 1890, six cases of a well-defined syndrome combining nervous and liver symptoms were published independently by *Gowers, Ormerod,* and *Homén.* Each author considered the disease-picture new and characteristic.

A. Strümpell, 1898-99, reported three more cases of pseudosclerosis and differentiated the symptomatology from multiple sclerosis. Although he found no significant brain lesions, he believed it was an organic nervous disease. He noted the hepatic cirrhosis in one case, but thought it syphilitic.

Bäumlin, 1901, first noted the familial tendency.

Frankl-Hochwart, 1903, published a monograph on pseudosclerosis. This ends the first stage in the evolution of the conception of the disease.

Between 1901 and 1911 there are only a few reports in the neurological literature, but in the ophthalmological literature *Kayser's* and *Fleischer's* studies advanced the knowledge of the symptom-complex. The neurological and ophthalmological lines here converge.

v. Hösslin and Alzheimer, 1912, discovered the characteristic microscopic lesions in the brain. They considered it a primary disease of the neuroglia.

Wilson, 1912, described it as a disease of the extrapyramidal system, connected the cerebral and hepatic lesions, advanced the theory of an endogenous toxin, and termed the disease progressive lenticular degeneration. He was unaware of the corneal ring.

Casemajor, 1913, reported a clinical and pathological picture resembling hepatolenticular degeneration and caused by manganese poisoning.

Rausch and Schilder, 1914, *A. Strümpell*, 1916, *Dziembowski*, 1917, studied the familial incidence.

Thomalla, 1918, found enlarged spleen, cirrhotic liver, and degeneration of putamen in a case of torsion spasm.

v. Economo and Schilder, 1920, described a disease resembling pseudosclerosis in the presenium and discussed its relationship to paralysis agitans.

Hall, 1921, in his monograph collected 68 cases (21 with ring) reported between 1912 and 1920. He discussed all aspects of the disease and introduced the term hepatolenticular degeneration. He considers the disease an abiotrophy and discussed the mechanism of inheritance.

Richter, 1923, developed the concept of the disease as an abiotrophy.

Barnes and Hurst, 1925, stressed the importance of attacks of acute hepatitis.

Kehrer, 1925, in a classification of the hereditary nervous diseases, put pseudosclerosis midway between the blastomatous processes and the system diseases.

Lafora, 1925, discussed the late hereditary and familial form of pseudosclerosis.

Vogt, 1929, found an increase of copper in the liver in a case of pseudosclerosis with ring.

Haurowitz, 1930, also found an increase of copper in the liver and basal ganglia in two cases of pseudosclerosis, both having rings.

Levy, 1931, *Bielschowsky and Hollervorden*, 1931, further studied hepatolenticular degeneration as a heredodegeneration.

v. Braunmühl, 1932, hypothesis of the structure of the toxin.

Lüthy, 1932, the latest monograph on the subject.

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LECTURES ON MOTOR ANOMALIES

II. The theory of heterophoria*

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The question of the importance of heterophorias as the possible origin not only of eyestrain but also of various troubles either general or localized in different parts of the organism, has not been answered satisfactorily up to this day. One cannot be satisfied on the score that heterophoria exists to a certain degree as a physiological condition and the great majority of cases, even those with a considerable amount of heterophoria, do not complain of any discomfort at all. If one is in the commendable habit of carrying out a thorough examination of the eyes of all patients, regardless of the trouble for which the ophthalmologist is consulted, one will very frequently find some kind of heterophoria that has produced no subjective symptoms. On the other hand, there is no doubt that heterophorias of a relatively small amount may cause manifold, even serious trouble, which is evidenced by the prompt disappearance of the symptoms after the correction of such phorias.

Why do different people react differently to phorias of equal kind and of the same degree? Before this question can be discussed one must state the exact meaning of the term heterophoria, about which the ophthalmologists seem still to be at variance. They agree with one another in so far as they understand heterophoria to be a latent squint that becomes manifest under certain conditions, either spontaneously—for instance, if the individual is tired or exhausted—or if binocular fixation is prevented artificially during the examination of the eyes. It is obvious that a sharp demarcation between squint and heterophoria does not exist. In cases of so-called periodic squint the deviation is manifest at times, while at others it is latent, according as to whether the fusion tendency is strong enough to overcome an anomalous position of rest or is weakened by fatigue, exhaustion, or anything else. Further, after one eye has become blind or amblyopic, due to disease or injury, a permanent squint will appear not infrequently in cases which had never before manifested a temporary deviation or subjective symptoms of heterophoria. In papers or discussions about heterophoria this term is frequently used to denote all types of deviation arising after binocular fixation is made impossible temporarily during the examination, while other authors who regard heterophoria as an anomaly of the anatomic position of rest argue that temporary deviations caused solely by inadequate—that is, either insufficient or excessive or other anomalous—innervations are not true heterophorias and must, therefore, be distinguished from these by different names. Thus, for instance, they claim that one should not use the term "exophoria for near" if there is orthophoria for distance. Such a condition should be called convergence insufficiency, since it is not due to an anomalous position of rest. Likewise, latent or temporarily manifest convergent squint which can be transformed into an orthophoria by an exact correction of an existing hyperopia should not be called esophoria, since it is pro-

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duced exclusively by an excessive convergence innervation associated with a corresponding accommodative effort required because of the hyperopic refraction.

The demand for an unequivocal nomenclature favoring the distinction between deviations of anatomic origin and those caused by innervational anomalies is all the more justified, since in many instances a different etiology may indicate a different treatment. If the term "exophoria" is used for both a divergent position of rest and a convergence insufficiency, causing a relative but not an absolute divergence in near work, the novice may be easily misled to operate in a case of the latter kind. This would be a mistake, for an operation in a case of orthophoria would bring about an esophoria for distance, and the improvement obtained for near work would not outweigh the impairment of the conditions for distance, the postoperative esophoria producing either homonymous diplopia or eyestrain due to the necessary effort to overcome the convergent position of rest. Formerly, an analogous mistake was made very frequently, before the relation between hyperopia and esophoria, respectively to convergent strabismus, was discovered by Donders. In many cases of convergent squint brought to operation by ophthalmologists who disregarded the hyperopia, a postoperative exophoria or a divergent strabismus was the result, because the primary convergence was not based on mechanical imbalance due to anatomic conditions, but on an excessive convergence innervation induced by an excess of the accommodative impulse. Thus, from a theoretical as well as from a clinical point of view, it seems advisable to distinguish between anomalies of the position of rest, and those of a nervous origin, or rather of a compound etiology. This requirement could be satisfied by an exact determination of the position of rest.

It is obvious that the anatomic and physiologic factors which are decisive for both the position and the motility of the eyes are to be separated into two groups, according to whether they have a mechanical or a nervous influence on the position of the eyes. The first group is represented by the topographic anatomic relations between the eyeballs and their adnexa—that is, the lids, the conjunctiva, the muscles, their course, length, and insertion into the sclera—further by the physical qualities of the muscles and of the fascial ligaments, the quantity of the retrobulbar, fatty and other intraorbital tissues, and finally by the size and the form of the orbits and the bulbi. Only if these anatomical conditions were absolutely identical on both sides could an ideal position of rest (orthophoria) be expected: parallelism of both the visual lines and the corresponding meridians of the eyes in distant vision. But, in view of the physiological asymmetries of both sides of the face it is obvious from the very beginning that the anatomic conditions within the two orbits, as a rule, will not be identical but more or less different; hence the ideal position of rest will not be the rule but an exception, just as the ideal refraction, namely, real emmetropia, is the exception, a certain amount of ametropia being the rule. Thus, the position of the eyes, so far as it depends solely on the topographic-anatomic, or mechanical, conditions would, almost without exception. result in a strabismus, one visual line deviating from the fixation point in one direction or another unless the fusion apparatus would prevent it by producing and maintaining a so-called compensating innervation by which the anomalous position of rest is kept latent and binocular fixation is attained.

Apart from the fusion innervation the

eyes are influenced continually by other innervations. We know some of these: the voluntary impulses, the association between accommodation and convergence, the connections between the different cortical sensory and the oculomotor centers, the connections between the vestibular apparatus and the oculomotor nuclei. That there is no position of the eyes where the muscles are totally relaxed has been ascertained by Hering, who, with the aid of a stethoscope, heard a continual humming sound in every position of the eye, indicating unsteady but permanent contractions of the ocular muscles due to the general reflex muscle tonus. Furthermore, we know from clinical observations that the position of the eyes very frequently, but neither constantly nor equally, is influenced by other innervations, which will be discussed presently.

Considering the number and variety of nervous factors which influence the eyes, it is easily understood that an exact determination of the anatomic or *absolute* position of rest—that is, the position of each eyeball within the orbit—is practically impossible, because the totality of nervous influences cannot be eliminated in any way. Only some of these can be eliminated completely or approximately: the voluntary and, to a certain degree, also the vestibular innervations, by cutting out the movements of the eyes, of the head, and of the body during the examination; moreover, the influence of accommodative efforts on the convergence innervation by the correction of any existing hyperopia and by the selection of a distant point of fixation. The increased tonus of certain muscle groups produced by the fusion innervation in cases of heterophoria can be relaxed more or less according to the procedures still to be discussed, but in no case can one be sure how long the aftereffect of the fusion innervation will last after the fusion tendency has been broken. The reflex muscle tonus can be eliminated no more than can certain innervations of unknown origin. Thus, being unable to determine accurately the absolute position of rest, one must be satisfied to ascertain the relative position; that is, the position of the eyes relative to each other which is displayed after as many of the nervous influences as possible have been eliminated. This is generally sufficient for clinical purposes; namely, for answering the question of whether, or how great a portion of the latent squint is due to anatomic or to nervous factors.

In examining the relative position of rest one must bear in mind that the result depends on certain conditions which cannot always be controlled or eliminated. If heterophoria tests are repeated several times under apparently equal conditions, the results obtained in those tests will very frequently differ and this not only with respect to the amount but occasionally also with respect to the kind of existent heterophoria. In a case of exophoria, for instance, the double images in the second test may be found to be further apart or closer together than in the first or the third test, and in the fourth test they may display a vertical separation in addition to the lateral one. Such a behavior is similar to that found when the amount of hyperopia, in testing young people, is to be determined without atropine. They cannot be induced to give up completely the increased tonus of the ciliary muscles by which they overcome the hyperopic condition of the eyes. Convex glasses of gradually increasing power will, in the beginning, make the ciliary muscles relax correspondingly. But the convex glass beyond which one cannot go without reducing the visual acuity will very often differ in several examinations; from which one must infer a correspondingly different relaxation of the ciliary

muscles in the different tests. If the individual is strong and animated, the manifest part of the hyperopia will, as a rule, be found to be smaller than it is if the same person is tired or weakened by illness. The same is true, *mutatis mutandis,* in cases of phoria. The increased tonus of those muscles, the contraction of which holds the squinting position in check, is not relaxed equally if the fusion tendency is broken in the same way, but at different times. As was mentioned before, it is one of the characteristics of the fusion innervations that the artificial temporary heterophoria produced by adequate fusion stimuli—namely, by a gradually increasing displacement of identical retinal images from corresponding to disparate points—does not disappear immediately after that stimulation has ceased. If prisms are used in the experiment, the eye behind the prism will be deviated in the direction of the prism apex. If the prism is removed after it has been worn for some time, binocular single vision will be restored after a few seconds of seeing double. But the suspending of fusion by a dark-red glass held before one eye after the removal of the prism causes diplopia and uncovers a fraction of the heterophoria which had been produced by the experiment. And if, after an interval of several minutes, the red-glass test is repeated, the same type of heterophoria, though gradually decreasing, will again be disclosed. As a rule, it takes 15 to 30 minutes for orthophoria to return. But even then a small residue of the artificial heterophoria may return and be displayed by later repetitions of the Maddox-rod or the red-glass test, particularly if the prism had been worn for some hours or days.

One learns from this experiment that a so-called compensating innervation of the eyes maintained by the fusion apparatus does not disappear immediately after fusion is broken, but decreases very slowly, and that not always without a temporary recurrence of a fraction of the fusion innervation. In the face of such behavior one can understand that a fusion innervation, used since early childhood to overcome an anomalous position of rest, will be much more resistant than any innervation produced by the vergence test, and that during temporary suspension of binocular vision only a fraction of the heterophoria will become manifest, a greater or smaller fraction, according to circumstances the nature of which very frequently cannot be explained satisfactorily. On the other hand, a squint practically always develops gradually when the fusion tendency is abolished through injury or disease, leaving behind amaurosis or considerable amblyopia of one eye. In those cases it is due mainly to the varying positions of rest that both the kind and the angle of squint differ; in the majority, divergent squint arises. In children up to 15 years, a convergent strabismus develops after the loss of binocular vision five times as frequently as in people of 30 years or more. This fact leads to the assumption that in adolescence there is a gradual change of the topographic-anatomic factors, resulting in a more divergent or a less convergent position of the eyes. Very frequently a lateral deviation is combined with a vertical or a rotary component, all showing the concomitant type in so far as the angle of deviation remains practically constant in the whole field of fixation, in contradistinction to a paretic or spastic deviation where the amount of the deviation changes, as a rule, corresponding to the direction of gaze. In the majority of cases in which the fusion tendency has been abolished, the deviation becoming manifest and displaying the relative position of rest will be less than 2 degrees and, as a rule, will no longer

change after the expiration of some weeks or months. Considering the fact that in many cases where, prior to the one-sided impairment or loss of vision leading to a manifest deviation, only a fraction of the latter, if any, could be displayed by the usual methods of investigation for heterophoria, it seems obvious that a complete relaxation of the fusion innervation cannot be obtained by these methods because the fusion tendency is not interrupted long enough for the whole amount of heterophoria to become manifest. In view of these facts Marlow[1] recommended the prolonged occlusion test of one eye. He found, in numerous cases, that the angle of deviation increased in accordance with the length of time the bandage had been worn. After a week, according to Marlow, the deviation will be found to be constant. But there are patients who then show a smaller degree of squint than was found before the bandage was applied, and some few in whom the kind of deviation at the end of the occlusion period was found to be opposite to that before the occlusion.

According to later publications by Abraham,[2] Beisbarth[3] (1932) and Marlow[4] himself (1933), the results of the occlusion test differ with regard to the amount as well as the kind of heterophoria, depending, not infrequently, upon which eye had been bandaged. In 49 out of 82 patients Marlow found as a result of the alternate occlusion, hyperphoria of the same kind but of a different degree; in 32 cases (that is, in more than 28 percent) there was also a different type, each eye, when uncovered, moving upward. Similar conditions were found in exophoria and esophoria. In 16 patients who first had the left and then the right eye occluded, the amount of exophoria found by the first test was reduced by the second test. In one test esophoria by the first occlusion was diminished from 10 to 6 degrees, whereas the occlusion of the second eye produced an increase to 15 degrees; that is, a higher amount than that which was found by the preocclusion examination.

These facts seem to prove that even the interruption of binocular vision for a week is not sufficient to uncover the relative position of rest. It is obvious that the different results obtained by the prolonged occlusion test in one and the same person, according to whether his right or his left eye has been bandaged, are to be attributed to peculiar—because unsteady and intermittent—innervations that alter the position of the eyes relative to each other in an incalculable way. Such innervations, indeed, occur not infrequently. In extensive investigations concerning the position of rest in normal people, as well as in people suffering from eyestrain or any kind of nervous trouble, I found about the same incidence of heterophoria —more than 80 percent—and in more than 41 percent of the cases the heterophoria was combined with an apparently dissociated vertical deviation, each eye, when covered, moving upward (fig. 7) or, while the other eye was fixed continually on an object, instead of keeping to a certain degree of deviation, slowly moving up or down at irregular intervals, occasionally even passing the horizontal plane in the downward direction.

Obviously, such an anomaly differs fundamentally from the concomitant as well as from the paretic type of vertical deviations in which, if the screen is put first in front of the right eye and then before the left, one eye will deviate upward and the other downward. The apparently contradictory results obtained by the aforementioned authors with the alternate occlusion test in a relatively high percentage of hyperphorias cannot be explained other than by assuming that those cases belonged to the group of dis-

sociated or alternating hyperphorias (fig. 7) previously mentioned, based not, or only to a subordinate degree, upon an anomalous position of rest—that is, on mechanical conditions—but on intermittent nervous excitations of the vertical motors, the origin of which is not yet known to us. This anomaly, first mentioned by Schweigger,[5] Stevens,[6] and Duane[7] must be discussed a little more in detail, for it is a frequent complication of the typical concomitant, as well as

Fig. 7 (Bielschowsky). Alternating hyperphoria; visual lines either parallel (a) or deviated upward alternately (b, c).

of the typical paretic motor anomalies of the eyes. I have been able to prove by the thorough investigation of many hundreds of cases that the aforementioned authors' interpretation of that anomaly—namely, that it is based on a muscular imbalance between the elevators and depressors, the elevators being considered stronger—was wrong. The assumption that the elevator muscles of either eye are stronger than the depressors cannot be reconciled with the fact that the upward deviation of the covered eye is not only inconstant but is sometimes transformed into a deviation of the opposite kind. This happens either spontaneously at irregular intervals, or may be produced experimentally by the doctor. If one puts in front of the fixating eye a darkening glass wedge (Zeiss), moving it in such a manner that the fixed lamp is gradually darkened, the covered eye which is first deviated upward, will be seen behind the cover to move downward below the horizontal plane, sometimes in almost exact proportion to the darkening of the fixating eye, which is continually keeping fixation during the examination. Numerous observations and experiments performed in the cases under discussion and described in my extensive publication concerning the dissociated vertical movements of the eyes,[8] made me believe that the great variety of signs and symptoms is due to alternating and intermittent excitations of both centers for vertical divergence; the onesidedness of the vertical movements in some cases is based on the coincidence of the voluntary fixation impulse with the involuntary action of one of the vertical divergence centers, so that the fixating eye keeps its position unaltered, since the innervations of the elevators and depressors neutralize each other in this eye. These cases must not be confounded with cases of periodic lateral or vertical squint in which one eye turns out or up when the patient is fatigued or diverted, and returns to binocular fixation by a unilateral movement as soon as his attention is attracted by an object that is situated in the visual line of the other eye. Some of these persons have learned to perform unilateral movements of one eye voluntarily or at command, but in all such cases a careful examination has shown that the unilateral movement is produced by bilateral and equal motor innervations, one driving both eyes in the same parallel direction,

while the other drives the eyes in the opposite direction. In these cases the fusion power plays the principal part in producing this kind of monocular movement. If the fusion power is eliminated or weakened the patient is no longer able to move that eye back from the squinting to the normal position. In contradistinction to these cases the one-sided vertical movements of the dissociated type have nothing to do with the fusion apparatus, for they are frequently found in patients with a permanent concomitant, convergent, or divergent, or vertical squint (figs. 8, 9). The retinal images of the squinting eye are either totally suppressed or they are not perceived on account of a high amblyopia. Nevertheless, this eye can be seen to move up and down at irregular intervals, so that now, for instance, it is deviated outward exclusively, then out and up, or out and down, but is never directed to the point fixated by the other eye. Only if one succeeds in correcting the anomalous position of rest so that binocular single vision is restored, may the vertical monocular movements due to the anomalous nervous excitations cease, the fusion innervation being stronger than the anomalous innervations arising from the vertical divergence centers.

With regard to the therapeutic procedure, it is very important to differentiate between the hyperphorias based on anatomic conditions—that is, on an anomalous position of rest—and the dissociated vertical deviations of nervous origin, since these should not be operated on, whereas an operation may be considered if the vertical deviation were due to an anomalous position of rest. I have seen patients with this type of dissociated hyperphoria before and after operation, for instance after recession of the superior rectus muscles. Of course, the position of rest was changed, but the range of the irregular vertical deviation was only transferred downward while its amplitude remained approximately the same as before the operation. There is no need for treatment in cases of pure alternating hyperphoria if the patients are endowed with good fusion power which masters the anomalous innervations without difficulty so that at most there is merely a temporary deviation when they are fatigued. And, as a rule, the degree of vertical deviation in the case of unilateral amblyopia is small and therefore not disfiguring. That anomalous excitations of the centers driving the eyes in opposite directions play an important part in the etiology of phorias and squint must be assumed not only because of the dissociated vertical deviations which have just been discussed but also for other

Fig. 8 (Bielschowsky). A, convergent strabismus, right eye. B, right eye turned up and in, after having been covered for a moment; left eye remaining in the primary position.

Fig. 9 (Bielschowsky). A, paralytic divergent strabismus of right eye. B, the right eye deviated up and out. C, the right eye deviated down and out, while the left (fixating) eye maintains its direction unaltered.

reasons. Excessive convergence as well as excessive divergence innervations, which are responsible for the corresponding types of squint in certain cases, will be discussed later on. Among the different kinds of heterophoria, the hyperphorias require the most thorough discussion, not only because of their frequency and the subjective troubles for which they are believed to be responsible, but even more because of their different nature. This must be cleared up, in order to find the best or the only way of correcting them.

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STUDIES ON INCLUSION BLENNORRHEA*

II. Expressional transmission

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Saint Louis

Introduction

The demonstration of cytoplasmic inclusions in the epithelial cells of the conjunctiva during the course of inclusion blennorrhea, by Stargardt[1] and Schmeichler,[2] was soon followed by the realization that the disease is distinct and separable from gonococcal conjunctivitis and indeed constitutes a clinical entity in its own right. This observation, repeated and confirmed a number of times by different observers, stimulated a prodigious amount of investigation of the etiology of the disease. For the most part this research converged on the significance of the inclusion body and the relation of inclusion blenorrhea to trachoma, since in the latter condition indistinguishable inclusions are also present. Up to the time of the World War, when the researches were thrown into an abrupt cessation, the predominant but not universal opinion predicated the inclusion body to be the causative agent of the infection, and maintained that trachoma was either a closely related disease, or in some indefinable way even an aberrant manifestation of the same agent. More recently, etiological studies have been resumed, and Thygeson[3] has brought forward valuable evidence to sustain the concept that the elementary body of the inclusion is the virus of inclusion blennorrhea.

Undertaking a study of this disease in this laboratory in continuity with the work on trachoma, the writers found it necessary to repeat a number of experiments already described in the literature and to extend them when warranted. On other occasions, experiments have been performed for the first time, with the purpose of crystallizing out from the still fluid state of confusion and contradiction information bearing on the nature of inclusion blennorrhea. In their respective places, appropriate acknowledgment will be made of the studies of our predecessors, whose results have facilitated and expedited this investigation. That the observations made may be presented more readily for discussion, it is proposed to limit this communication to the experiments on transmission, and to reserve for a later report the data bearing on the nature of the infectious agent.

Methods

Material. Material for study was obtained for the most part from patients attending the ophthalmological clinics of Washington University; three patients were furnished by the Saint Louis Maternity Hospital. After removal of most of the pus by soft cotton gauze, sometimes supplemented by short irrigation, the eye was anesthetized with holocaine or pontocain. Everting one lid at a time, the conjunctiva was scraped with a sterilized Lindner platinum spatula, and the tissue thus removed was emulsified in veal-infusion broth (pH 7.6). Scrapings from the four lids were usually suspended in about 1.0 c.c. of broth, and varying quantities of blood were also transferred by this technique. It was possible to return to the patients a number of times at intervals of a few days or a week, and thus to obtain a relatively large yield of material

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from some of them. Most of the studies were made with material obtained during the acute stage.

Inoculation of animals. Since materials were obtained in the same building, it was possible to complete all animal inoculations within a matter of minutes and thus avoid delay from patient to animal. Inoculations of the conjunctiva were made by direct swabbing on some occasions, but in general the method of injection was preferred. This was accomplished by multiple pricking of the conjunctiva with a charged needle, allowing material from the syringe to drip over the scarified area and then introducing about 0.2 c.c. of the suspension subconjunctivally.

Experimental

Preliminary experiments were conducted to determine the transmissibility of an infectious agent from infants with inclusion blennorrhea to various animals. Inoculations of human material were made both conjunctivally and by different routes in rabbits, guinea pigs, and rats. Since no gross evidence of infection was detected after several trials, no further attempts at transmission were made. Among the different expedients studied, infectious material was injected intratesticularly into rabbits without inducing clinical changes of any note. Impression smears and histological sections of the inoculated testicles revealed no particular information, and no structures simulating the inclusion or its constituents were ever observed.

Because it had been suggested[3] that the elementary body of inclusion blennorrhea may be analogous to the elementary body of psittacosis, repeated efforts were exerted in adapting to this study the technique so successful in demonstrating and isolating the virus of psittacosis.[4, 5] Accordingly, white mice, Swiss mice, and Bar Harbor mice (C-57) were all used. Conjunctival material from several patients was inoculated intraperitoneally, and the animals were killed at daily intervals up to five and seven days, since they had tolerated the injections with no apparent effect. Smears were made from the peritoneum, the exudate being sufficient, particularly after the first and sometimes even the second day. Material from the peritoneal cavity was also obtained by scraping the peritoneal walls. Smears were then made of the different organs, the spleen being studied in great detail by series of impression smears. The different preparations were later stained by Giemsa and Castaneda-Rivers stains,[5] but at no time were any structures found to indicate the presence of infection referable to inclusion blennorrhea. Sections of the spleen later confirmed this conclusion.

In order to increase if possible the virulence of the infectious agent, peritoneal washings from mice inoculated on previous days were injected in series from mouse to mouse for six to eight passages without obtaining any indication of carrying the agent. In fact, the peritoneal washings, relatively heavy after the first passage, became more and more watery, until cells of any kind were found with difficulty. It was obvious after three such experiments that material of a given infectivity for humans acquired no infective capacity for mice by successive passage.

In another group of mice, inoculations of material were made intracerebrally without clinical effect. When killed at the end of the week, no sign of infection was demonstrable either by macroscopic or microscopic methods.

In summary, then, it seems justifiable to state that neither inclusion blennorrhea nor its infectious agent is transmissible to the smaller animals. This is in agreement with similar observations made on a lesser scale by Thygeson.[3]

Transmissibility to monkeys. That in-

clusion blennorrhea is transmissible to apes and monkeys was established by a number of workers in the past. The earlier observers, however, were interested not so much in the transmissibility of the disease as in the occurrence of inclusion bodies in the infected animal and their relation to those of trachoma. Consequently, the information to be gained from their reports on the clinical phases of the experimental infection is lacking in detail. However, in table 1, a summary is given of experiments undertaken by past workers on transmission to apes and monkeys, and, while it is not always clear that the animals were infected in each instance recorded, the author's opinion has been respected. This table includes transmissions attempted only with unaltered material from the human to the animal eye, so that inoculations from animal to animal, or with material from the human eye altered by filtration, heating, storage, and so forth, or with material from the genital tract of the patients' parents have been excluded. The data indicate that Lindner[6] was the first to attempt transmission to monkeys and apes when he successfully infected a *Macacus rhesus* and a baboon. These results were subsequently confirmed by several observers, so that a total of 58 animals have been infected experimental-

TABLE 1

COLLECTED DATA ON THE TRANSMISSIBILITY OF INCLUSION BLENNORRHEA TO APES AND MONKEYS

Observer	Date	Number of Animals		Period of Incubation
		Inoculated	Infected	
Lindner[6]	1909	M. rhesus 3	1	6 days
		Baboon 1	1	5 days
Flemming[7]	1910	M. rhesus 1	0	
		Baboon 1	1	7 days
Fritsch, Hofstätter, & Lindner[8]	1910	M. rhesus 1	0	
		Baboon 1	1	7 days
Heymann[9,10]	1911	M. rhesus 1	0	
		Baboon 5	5	5 to 10 days
		Cercopithecus 5	5	4 to 7 days
Morax, Lindner, & Bollack[11]	1911	Baboons 4	3	4 and 5 days
Boeing[12]	1912	Cercopithecus 2	0	
Botteri[13]	1912	M. rhesus 1	0	
		Baboon 1	1	3 days
Löhlein[14]	1912	M. rhesus 1	0	
		Baboon 2	2	one, 14 days
				one, <21 days
James[15]	1930	M. rhesus 1	1	12 days
Thygeson[3]	1934	M. rhesus n.s.	6	n.s.
		Baboon n.s.	2	n.s.
		Sooty mangaby 1	1	n.s.
Tilden and Gifford[16]	1936	Baboon 2	2	12 & 16 days
Present report	1938	M. rhesus 45	25	5 to 13 days
		Baboon 2	1	5 days

n.s. = not stated.

ly, judged on the basis explained. Almost half this number are the animals recorded from this laboratory. The number of infected animals includes 33 of more than 54 *M. rhesus* inoculated, 19 of more than 19 baboons inoculated, five of seven cercopithecus inoculated, and one mangaby. It would appear, therefore, that on collective evidence *M. rhesus* is the most resistant to infection of the species tested. The percentage of successful transmissions in this disease appears to be higher than that obtained by various workers in the transfer of trachoma to animals.[17] It was, therefore, established before this work was undertaken that inclusion blennorrhea is transmissible to apes and monkeys, following a period of incubation fluctuating between 3 and 21 days, irrespective of the animal infected.

Character of the experimental infection in animals. It has been possible in this laboratory to transmit inclusion blennorrhea to monkeys either directly from patient to animal by swab, or as described above with a suspension of scraped tissues inoculated by swabbing or by injection. In this manner, 25 monkeys and 1 baboon were successfully infected with unaltered material, and the character of the experimental infection was similar in all animals, the variations encountered being mainly of severity or extensiveness. During the first few days following inoculation of the human tissues, there was a varying, but never a marked, degree of mucopurulent discharge, mild hyperemia, slight congestion, and occasional swelling of the lids. This, however, was not regarded necessarily as a prodromal manifestation, for it happened frequently even in animals that were eventually considered unaffected by the inoculation. The exudate was essentially polymorphonuclear and may well have been due to the opportunistic bacteria so frequently present in the human material, although it must be stated that organisms were never observed in great numbers in smears of the discharge, and, in fact, they were frequently not found at all. This reaction subsided, in general, within 3 to 5 days.

The phenomenon by which infection was determined was the appearance of follicles. These were detected singly or in small clusters as small, translucent, discrete and circular elevations appearing first in the retrotarsal folds of either the upper or lower conjunctiva. The follicles then increased in number and were characterized by uneven distribution, variation in size, and, in some, marked vascularization sufficient to give the whole follicle a red coloration. Reaching a maximum within a week or two, the infection arrived at a chronic stage at which the general appearance remained unchanged until healing set in. At this time the follicles began to recede gradually, and the time required varied considerably in the different animals. The reaction was always follicular, never papillary, and the tarsus, bulbar conjunctiva, and cornea were never observed to participate in the infection. In some animals there seemed to be a tendency to greater involvement of the lower lids, but this was too irregular to be regarded as a typical development. Upon recovery, the conjunctiva became pale and smooth, resembling in every way the normal tissue. In the one baboon (var. Sphinx) infected, the reaction was similar to that observed in *M. rhesus* monkeys except for an unmistakably greater folliculosis of the lower conjunctiva. As far as could be determined, experimental inclusion blennorrhea[18] in monkeys is indistinguishable clinically from experimental trachoma. In fact, it is our experience that not only are these diseases the same in monkeys, but experimental swimming-bath conjunctivitis also presents an undifferentiated clinical picture.[17]

In order to portray the clinical develop-

ment of experimental inclusion blennorrhea, a table (table 2) has been made of the reactions in 25 successfully infected monkeys. If, as indicated above, the appearance of follicles be accepted as the first tangible evidence of specific infection, then the period of incubation will be found

TABLE 2

EXPERIMENTAL INCLUSION BLENNORRHEA IN 25 MONKEYS (*M. rhesus*)

Period of Incubation	Number of Monkeys	Duration of Disease	Number of Monkeys
5 days	3	2 weeks	1
7 days	11	3 weeks	3*
9 days	2	4 weeks	4
10 days	1	5 weeks	3**
11 days	3	6 weeks	4
12 days	4	2 months	5*
13 days	1	3 months	1
		4 months	1
		5 months	1
		7 months	2

* Includes 2 monkeys dying at this time but with active conjunctival lesions.

** Includes 1 monkey dying at this time but with active conjunctival lesions.

to occur within 5 to 13 days, which is in harmony with observations of past workers (see table 1). Slightly more than half the animals, however, became infected within a week following inoculation of human material. This period is shorter than that observed in experimental trachoma, where the variation extended from a few days to more than a month, with 2 to 3 weeks forming a fair average. The duration of the experimental infection also showed great variations, the disease lasting as little as 2 weeks and as much as 7 months, with more than half the animals recovering completely within 6 weeks. This is again in contradistinction to the condition in experimental trachoma, where the infection is considerably prolonged, lasting in rare instances to 3 years and more, but in half the monkeys spontaneously healing within 6 months.[18]

The impression gained, therefore, is that inclusion blennorrhea is transmissible to monkeys as a mild infection characterized by a state of folliculosis indistinguishable in appearance from experimental trachoma and experimental swimming-bath conjunctivitis. It differs from experimental trachoma in a shorter period of incubation, and considerably diminished duration, which is evidence of its mildness. Other similarities and contrasts between the two infections will be brought out later.

Histologically, tissues removed during the experimental disease revealed similar changes in all animals, the only differences being those ascribable to severity of infection. Varying in size, the follicles were composed of small lymphocytes and plasma cells occasionally surrounded by a thin collar of fibroblasts. In earlier stages, the conjunctival epithelium was frequently in the process of desquamation, and many individual cells showed a swelling and ballooning. Later, as the infection became chronic, the epithelium was regenerated, but, due to the size of certain follicles, it was thrown into invaginations. Scar tissue was never seen, nor did careful search ever disclose epithelial inclusions *in situ*. Thus, the histological changes cannot be differentiated from those disclosed, for example, in experimental trachoma.

Infectivity of different patients with inclusion blennorrhea. The degree of infectivity of tissues from different patients may show distinct variations. In order to illustrate this point, data have been assembled in table 3 of 19 different experiments performed with tissues from 19 patients. Unlike former experiments in this laboratory on trachoma, where it was frequently found convenient to pool tissues from different patients, material from each individual was employed singly for each experiment, thus allowing a more accurate analysis of the data. While the day of the disease on which tissues were

obtained is given, it is now obvious that infectivity is affected not so much by the age of the disease as by the clinical stage. In a general way, therefore, tissues obtained early during the infection are more infectious than tissues obtained later, provided the earlier period is still during the active stage. Consequently, while the majority of monkeys were infected with material derived from patients up to 5 days following onset, the data reveal such wide extremes as a complete incapacity of tissues obtained on the 2d or 3d day of the disease to infect monkeys, and a measurable infectivity of materials representing the 4th week of inclusion blennorrhea. Some of this variation may be accounted for by differences in individual susceptibility of the monkeys inoculated, as will be brought out subsequently. Due to fortunate circumstances, it was possible to test the difference in infectivity in the same infant before and during an exacerbation of symptoms. In one patient, material was not infectious for monkeys when obtained towards the end of the acute stage at the close of the 2d week. During an exacerbation in the chronic stage, some 12 to 14 days following the termination of the acute stage, material from this patient caused typical infection in the two animals inoculated. In a second experiment, the demonstration was not so striking, since material obtained both at the end of the acute stage and during the exacerbation proved to be equally infectious (see table 3). Nevertheless, the one example may illustrate the point that infectivity depends not on the age of the disease, but rather on the activity of the infection. It may be of interest to add in this connection that the mere presence of inclusions does not imply infectivity for given tissues. In all the experiments performed, all the materials contained inclusions, in varying numbers. Only certain of the tissues, however, were infectious, indicating in another way the importance of the degree of clinical activity as a determining factor in infectivity.

TABLE 3

INFECTIVITY OF TISSUES FROM INCLUSION BLENNORRHEA

Age of Disease	Patients	Number of		
		Experiments	Monkeys in Each Experiment	
			Inoculated	Infected
2d day	1	1	2	0
3d day	3	3	2	0
			4	2
			3	1
4th day	3	3	3	1
			2	1
			2	1
5th day	4	4	2	2
			3	0
			4	4
			2	2
11th day	1	1	2	0
2 weeks	3	3	4*	0
			2	0
			3	3
4 weeks	2	2	2†	2
			4	2
*3d day after exacerbation	1	1	2	2
†5th day after exacerbation	1	1	2	2
Totals	19	19	50	25

* In this experiment, first inoculations made 2d week of disease did not induce experimental infection.

† In this experiment, first inoculations made 4th week of disease also induced experimental infection.

Variation in individual susceptibility of monkeys. That a certain degree of the observed variation in infectivity of the human tissues may actually represent a variation in the individual susceptibility of the animals inoculated was considered as more than likely because of such an observation in a previous study on trachoma. Consequently, the data were re-

studied to determine the likelihood of this possibility. As illustrative of the nature of the evidence, three individual experiments have been summarized in table 4. Thus it will be seen that in experiment IB-3, four monkeys were inoculated under identical conditions, but only two were infected. Although the period of incubation was the same, the duration was 6 weeks in one and 2 months in the other animal. So, in experiment IB-6, only one of three animals was infected. In experiment IB-15, again,

TABLE 4

VARIATION IN SUSCEPTIBILITY OF MONKEYS TO INCLUSION BLENNORRHEA
(3 Typical Experiments)

Experiment	Monkeys Inoculated	Period of Incubation	Duration of Disease
IB-3	# 80	not infected	
	# 87	not infected	
	#115	7 days	6 weeks
	#116	7 days	2 months
IB-6	# 21	not infected	
	# 57	10 days	5 weeks
	#125	not infected	
IB-15	# 40	7 days	6 weeks
	# 41	not infected	
	# 42	13 days	3 weeks
	# 43	not infected	

of four animals inoculated, only two were infected, with variations in the period of incubation of 7 and 13 days, and in duration of the infection, of 6 and 3 weeks, respectively. Thus, it is obvious that individual monkeys vary considerably in their susceptibility to experimental inclusion blennorrhea. Inoculated under the same conditions, with equal quantities of the same material, some animals become infected and others do not; those which are infected may in turn show variations both in the rapidity of onset and in the duration of infection. It becomes immediately apparent that, as in experimental trachoma, it is necessary that infectivity be studied on a more or less statistical basis if inaccuracies are to be avoided.

Serial passage of inclusion blennorrhea in monkeys. Because of the infrequency of inclusion blennorrhea, a consistent effort was made to establish the infectious agent of the disease in monkeys by passage from animal to animal. Experiments conducted by past workers have been somewhat incomplete, and while occasionally it has been reported that the infection is transferrable from animal to animal, the data are scanty and the series of passages was not so prolonged as seems desirable to the writers. Thus, for example, Fritsch, Hofstätter, and Lindner[8] carried the agent a single passage, as did Heymann[9] and Flemming,[7] also. Morax, Lindner, and Bollack[11] attempted four successive passages with apparent success in the first two; that is to say, the agent was lost during the third passage. On the other hand, a passage attempted by Boeing[12] was unsuccessful.

In this laboratory, four experiments were undertaken in this connection. In two experiments, it was not possible to carry the infection from the original animal to several monkeys. In two other experiments, infection was transmitted in the second passage, but not in the third passage. In the animals infected in the second passage, the infection was extremely mild. In each instance, material for serial inoculation was obtained while the lesions were still clinically active. It seemed, therefore, that despite the small number of experiments, it is not possible to adapt the infectious agent of inclusion blennorrhea to the conjunctiva of monkeys, since the agent either becomes lost or inactivated in these animals. Again, the behavior of inclusion blennorrhea in monkeys strikes a close resemblance to that of experimental trachoma. In this condition, also, it was shown in more extensive experiments that trachoma is not permanently adaptable to monkeys and that by the third passage the infectious

agent is usually no longer detectable by animal inoculation.[18]

The immune response of monkeys to inclusion blennorrhea. It was the opinion of Lindner[19] that following recovery from experimental inclusion blennorrhea, baboons enjoy a temporary (6 months') immunity not only to this disease but even to trachoma. Later, Thygeson and Mengert[20] repeated the experiment, and their results reveal that two baboons reinoculated, one 6 months and the other 4 months after recovery from experimental inclusion blennorrhea, developed typical disease, thus indicating a complete lack of immunity. In another experiment, three baboons, recovered from experimental trachoma, were found conversely to be susceptible to inclusion blennorrhea.

The number of experiments that can be done on the question of immunity to inclusion blennorrhea is limited because of the inherent difficulties of the problem. The infrequency of the disease does not always allow a supply of material when it is desired, and the lack of infectivity of the material to be used is not always predictable. Consequently, too long an interval may elapse between recovery and reinoculation, thereby possibly vitiating to some extent the value of the evidence acquired in such studies. However, in two experiments, all the proper conditions were met: in the first, two monkeys were reinoculated within 3 weeks of their recovery from the original infection and both animals became infected, one 7 days, the other 9 days after inoculation. In both animals the infection ran for about 5 weeks. In the second experiment, two more monkeys were reinoculated, one about 6 weeks and the other about 8 weeks following recovery. In both animals, infection again ensued. The periods of incubation were 5 and 10 days, and the duration about 4 and 6 weeks. It is clear, therefore, that animals recovering from inclusion blennorrhea do not necessarily acquire resistance to a second inoculation of infectious material, and that the second infection shows no significant deviations from the primary experimental disease. Again it is desired to point out the analogue in trachoma. Reports from this laboratory have already shown that monkeys recovering from the experimental trachoma are susceptible to reinoculation, undergoing an infection in every way similar to the first manifestations.

In order to complete the cycle, animals recovering from inclusion blennorrhea were inoculated with active trachomatous tissues, and animals recovering from trachoma were inoculated with tissues from inclusion blennorrhea. The results in both varieties of experiments indicated clearly that no immunity to the heterologous infection is demonstrable. This was, of course, to be anticipated. There is little reason to suppose that, impotent to stimulate an immunity against itself, an infection will nevertheless immunize against a heterologous agent. The present experiments, therefore, corroborate those reported earlier by Thygeson and Mengert.[20] The discrepancy in results between these experiments and those of Lindner is probably due to the variations in infectivity, pointed out above, that may accompany different tissues.

Transmissibility of inclusion blennorrhea to the genital tract. That inclusion blennorrhea may be an adaptation of a genital disease to the conjunctiva has been predicated by several workers on the basis of convincing clinical and experimental evidence. Thus, the cytoplasmic inclusions of the conjunctival cells have been found in the urogenital tract of parents whose infants suffered from inclusion blennorrhea.[21 to 23] Fritsch, Hofstätter, and Lindner[8] subsequently demonstrated that inclusion-containing material from urethritis in men and from the vagina of mothers with infected babies induced experimental inclusion blennorrhea when in-

oculated in the eyes of baboons. This observation was confirmed by Heymann,[9] and somewhat later by Thygeson.[8] It remained for Lindner to complete the chain of evidence by demonstrating that material from inclusion blennorrhea might be inoculated into the vaginal canal of a baboon with a resultant vaginitis and the appearance of typical inclusion bodies. This experiment was repeated with similar results by Heymann.[9] Thygeson and Mengert[20] also attempted to infect two baboons from material from inclusion blennorrhea, the inoculation resulting in a definite cervicitis, but inclusion bodies were not demonstrable, so that the inflammation may have been nonspecific. Similarly, they also inoculated four women in the last months of pregnancy, the inoculation inducing no effect either in the women themselves, or later in their infants. Two other women, inoculated prior to the onset of labor, showed no response, and their infants born shortly after were also free of infection.

A similar attempt was made in this laboratory to infect animals by way of the genital tract. Four *M. rhesus* monkeys and one baboon were inoculated with active material containing inclusions. Inoculations were made first by vigorous swabbing of the vaginal folds and uterus with human tissues, and then after scarifying the vaginal and uterine walls with a charged needle, material was injected intra- or subcutaneously. The animals were kept under observation for 2 to 3 weeks. Physically, the animals gave no clear signs of inflammation, and scrape smears examined periodically during the interval were apparently lacking in inclusion bodies.

Transmissibility of inclusion blennorrhea to the adult. In a subsequent communication, the transmissibility of inclusion blennorrhea from human to human will be dealt with in detail, because this subject will be introduced in a special connection. It does not seem necessary at the present time, therefore, to say more than that the disease is transferable to the adult conjunctiva. Here it manifests itself in somewhat different form, and it reproduces the spontaneous condition clinically recognized as swimming-bath conjunctivitis.

Discussion

The experiments described and reviewed in this communication demonstrate the transmissibility of inclusion blennorrhea to apes and monkeys. Unable to establish itself in lower animals, such as the rabbit, guinea pig, rat, and mouse, it appears in monkeys, however, as a follicular conjunctivitis following a period of incubation averaging about one week. The experimental disease continues as a chronic infection, eventually regressing completely within a few weeks to several months. Except for the relatively accelerated period of incubation and diminished duration, the experimental disease simulates the condition induced by trachomatous tissues, so that both manifestations become indistinguishable in the monkey. Again, like experimental trachoma, the infection leaves no trace of its previous presence upon recovery of the animal; it is incapable of successive transfer from monkey to monkey; and it confers no measurable immunity in the recovered animal. Certainly, on the basis of experimental infection in the monkey, the impression is readily gained that the two diseases are closely related and their infectious agents appear to fall within the same or closely allied biological group. This concept, however, will be developed more extensively in a subsequent report when experimental evidence will be available for more detailed discussion.

The experimental observations of other investigators (Fritsch, Hofstätter, and Lindner; Heymann; and Thygeson) leave little doubt that inclusion blennorrhea is

a divergent form of essentially a genital disease. Consequently, these workers have been able to induce experimental inclusion blennorrhea with material from the adult genitalia which contained the typical inclusion bodies. The attempts of Thygeson and Mengert,[20] as well as ourselves, failed to corroborate the observations of Fritsch, Hofstätter, and Lindner[5] that material from infants with inclusion blennorrhea may cause an inflammatory infection of the genital tract in the female baboon. This disagreement is in our opinion explainable on the ground of variations in infectivity of different tissues, as well as variation in susceptibilities of different animals, and even fluctuations in the relative resistance of different tissues (for example, conjunctiva and genital epithelium) in the same animal.

In either condition, conjunctival or genital, inclusion blennorrhea must be considered as a disease of low infective capacity. Its infrequent incidence, its occurrence in sporadic, isolated instances must imply its ordinarily difficult transmission, and that in all probability it requires massive doses of the infectious agent for implantation. So, in the animal, successful transmission demands relatively large amounts of recently obtained tissues, with the result that when serial dilutions of suspensions were made, the infectious agent was carried beyond its range of activity within a three- to five-fold dilution. Also suggestive of the low-grade infectivity of the disease is the fact that when normal animals were caged with infected monkeys, spontaneous infection was never observed in the normal individual.

Summary and conclusions

1. It has not been possible to infect rabbits, guinea pigs, rats, or mice with conjunctival scrapings from patients with inclusion blennorrhea, regardless of the route of inoculation.

2. Inclusion blennorrhea is transmissible to the monkey (*M. rhesus*) and the Sphinx baboon.

3. In these animals, there is an incubation period of 5 to 13 days, when a follicular conjunctivitis ensues and persists from a few weeks to several months.

4. Upon recovery, the follicles disappear, and the conjunctiva assumes its previous, normal appearance.

5. Tissues from different patients vary in infectivity despite the presence of inclusion bodies, and animals vary in their individual susceptibility to the experimental infection.

6. The infectious agent was not adapted to monkeys by serial passage.

7. Animals recovering from experimental infection acquire no immunity to reinoculation with active material.

8. Attempts to establish the infectious agent in the genital tract of the female monkey and baboon were unsuccessful, although the evidence of past workers indicates that this may be accomplished.

9. Experimental inclusion blennorrhea of monkeys is undifferentiated clinically or histologically from experimental trachoma.

10. Except for a general shortening of both period of incubation and duration in experimental inclusion blennorrhea, the two diseases must be considered the same in monkeys.

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THE VALUE OF ROUTINE IN EXAMINATIONS OF THE EYE*

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How many of us remember the emphasis placed on routine physical examination when we were in medical college, in sophomore or junior classes? We were instructed over and over to conduct all examinations in routine order, as only in that way could gross mistakes be avoided. The instructions were: "Always make examinations in a certain order: inspection, palpation, percussion, and an osculation." How many of us since then have been trying to find short cuts, because of the tediousness of routine? We recall the story of Osler who, on entering the ward with his assistants one morning, was shown a new patient, a sailor, suffering from headache: Osler cut his assistant short with the remark, "Sailor, headache, potassium iodide. Next case."

In many ways we should copy Osler, but not in his short cuts—until we are as wise as he. Routine is necessary. Take for example a mistake I made while assisting Dr. Wilder. One of his old patients came in with a cinder in his eye. As Dr. Wilder was quite busy, I removed it, and called him in when I was all through. He asked me if I had looked at the other eye. I said "No, there was no complaint of that eye." I then looked and found a cinder in that eye too!

Progress is made by studying our mistakes and taking steps to correct them; also, less painfully, by studying the mistakes of others and arranging to avoid them. To improve the technique of our routine is the purpose of this paper.

Routine is not a substitute for brains; it is an aid to our understanding of the patient. It has as much place in opthalmic practice as has the ophthalmoscope. Both should be used not blindly, but with judgment. Many years ago during a ward walk an adjunct in the clinic was handed an ophthalmoscope, through which I had just examined the anterior segment, using a +20 lens in the aperture.

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He was asked to look at the atrophic condition of the optic nerve, and he described the appearance of the nerve head without changing the lens in the aperture. Even an ophthalmoscope has to be used with judgment. So it is with routine.

The patient comes to the physician because of certain symptoms. He should be allowed to talk. His trouble is often best expressed in his own words. Sometimes he has to talk quite a while before the real cause of his visit can be ascertained. Dr. Sippy used to encourage his patients to tell their story several times—to the interne, to the assistant, to the associate, and to himself. It is natural when one is ill to want to tell the physician what's wrong. Encourage the patient to do this. Have enough room on the history card for a rather full résumé of the symptoms. Find out who the patient's general physician is—often a letter to him asking for more details will be a valuable contact in several ways. If a letter regarding the patient has been received, it and other family data should be at hand.

Next in order comes the objective examination. The vision is taken always of the right eye first, and always without glasses first. The various glasses brought by the patient are neutralized and the details about them recorded; for example, when and by whom ordered, whether the examination was made with or without cycloplegia, and like details. The vision and accommodative near point are taken with the patient's glasses and the difference noted from the normal for the patient's given age. Lowered accommodation (hypocyclosis) suggests the possibility of glaucoma. A manifest refraction, carefully done, with re-testing of the accommodative range and comparison of the accommodation of the two eyes will often give a clue to the conditions present. In 30 seconds more the Ishihara or a similar color test can be used, and additional information obtained.

Many mistakes seem to be due to failure to set down observations. For example, a person walks into a room with his head tilted to one shoulder, yet the fact is not recorded. Repeated failures in making such records lead to less observation, and this finally almost to ignoring the fact when it is seen.

A complete description of the external appearances of the face, lids, and eyes is next in order, including comparison of sizes of palpebral fissures in millimeters if they are different, presence or absence of pterygium and arcus senilis, color of irides, and reaction of pupils. A year or two before Dr. Wilder died he saw in consultation a patient with an obstinate conjunctivitis. I wondered why he wanted to double evert the upper lid, for I saw no reason for such procedure—until he had everted it. There was a typical follicular trachomatous condition. Routine examination had uncovered it.

The muscular balance must not be neglected—it naturally follows the inspection of the individual eyes. The importance of noting their relationship in all fields was emphasized many years ago by Dr. Alexander Duane in his masterly thesis for the American Ophthalmological Society. Dr. Duane spent many subsequent years perfecting the chapter on muscles incorporated in the last several translations he made of E. Fuchs's textbook. Subjective and objective examinations are made, not only for distance and for the near point (reading position) but in the various fields of action, the six cardinal positions. As he so often pointed out, the primary position tells us very little of the condition of any one muscle; all it can tell is a relationship between the various muscles. The importance of the six cardinal positions was again emphasized in Dr. James W. White's talk two months ago. He spoke for an hour on only one aspect of the problem. Careful and repeated study of the muscle chapter in Duane's Fuchs

will repay many times over in satisfaction. The technique of the cover test is not easily mastered, but obviously objectively obtained data are better than those obtained subjectively.

Case 1. In 1921, Mrs. A. C. I. presented herself with the complaint of inability to see clearly. She had always tilted her head to the right, but no record of this was made at the time. A 1$^{\Delta}$ left hyperphoria was found, but it was impossible to measure the duction power, as she would suppress either one eye or the other so readily that diplopia could not be induced at that time. Glasses which satisfied her were ordered, and were changed every three or four years, no prisms being incorporated until 1934. In January, 1934, cognizance of the head tilt was finally taken, and by combined cover test and red glass over one eye a paresis of the R. superior rectus and overaction of L. inferior oblique were demonstrated, and with the Maddox rod a reading of 4½$^{\Delta}$ left hyperphoria at distance in the primary position and 5$^{\Delta}$ at near point was obtained. A 3$^{\Delta}$ vertical prism was incorporated in her glasses and she wore these with considerable comfort for over three years.

Last spring (1937) she was seen again, and as there seemed to be no measurable stereopsis the prisms were removed. She was quite uncomfortable. The cylinder axis was changed, but without help. Two months later her husband telephoned requesting that the prisms be restored. This was done, with an increase in the prism to 4$^{\Delta}$ vertical and the addition of 4$^{\Delta}$, base in. The phorias as measured by cover test were 4$^{\Delta}$ exophoria increasing in eyes to the right, also in the eyes up and at near point; 6$^{\Delta}$ left hyperphoria increasing in the eyes to the right and up (spasm L. inferior oblique). Marked weakness of convergence was disclosed; PcB 200+. For a few days she occasionally had diplopia and some nausea, but since then has been quite comfortable wearing her glasses constantly.

Often in a hasty examination in the primary and reading positions we obtain data that seem to be well within normal limits, a few prism diopters of exophoria or esophoria. If, therefore, the nearpoint of convergence (the PcB) is neglected, some information may be lost. For with perfect refraction, and fairly satisfactory muscle balance, a lack of convergence power is often the cause of discomfort in reading. This is one condition that is readily amenable to treatment.

And before finishing the examination of the muscle balance one should investigate the ability of the patient to fuse the images; that is, the presence of 1st, 2d, or 3d degree of fusion; and if 3d degree, there is now a means of differentiating percentage depth perception.

Having gathered the data about the muscles they should be studied, and also what various authorities have said about similar data. This is easily said; it takes time from recreation, but it is fascinating.

Dr. Von der Heydt has continually emphasized the value of routine slitlamp examination. Often fluorescein staining will reveal unsuspected minute losses of epithelium. The state not only of the cornea and iris, but also of the anterior chamber should be set down in detail. The more one studies the angle of the chamber with a fine beam, the more one will see early pathology—adhesions, narrowing, deposits. This is especially true if an operation is in prospect.

Case 2. Recently an old patient was in the office. He was first seen in the spring of 1927 at the age of 67 years. He had a chronic noncongestive glaucoma of the left eye with tension 35 mm. Hg and was operated on twice, first with an iridotasis and later with a trephining. Over the iridotasis wound a dissecting bleb advanced on the cornea and was stopped by cauterizinig a fine line, which pro-

duced changes in Bowman's membrane just ahead of the bleb. On account of this he was shown at a meeting before this society about seven years ago. Subsequently he developed a guttate choroiditis and cataract, and now with the left eye is able to count fingers at 4 ft.; tension 5 mm. (Schiötz).

His history is presented at this time not because of the condition of the left eye, but of that of the right. From the first there was no suggestion of glaucoma, at least of a progressive nature, in the right eye. The fields, both central and peripheral, were suggestive, and as time went on they did not become worse—they were even improved. The tension was always low until on one occasion, four years ago, when it increased from 21 to 27 mm. Hg on the use of homatropine. The photometric test, which had been well within normal limits nine years ago, was not made at this time because of a developing guttate keratitis.

Recently he returned again complaining of colored halos about lights and with vision reduced from the former 20/20 to 20/40, unimprovable with glasses. The peripheral field was better than it had been formerly, and the enlarged blind spot was not greater. The tension, however, was 45 mm. (Schiötz). The anterior segment was normal, including an active pupil of 2½ mm. with normal depth of the anterior chamber, and no gross defects of the lens as viewed through the small pupil. There was a shallow physiological cupping of the optic disc, but also a slight glaucomatous halo.

When the pupil was dilated to 6 mm. with neosynephrin the tension was unaltered, but a typical shredding of the anterior capsule of the lens was seen; that is, the condition was a "glaucoma capsulare." The tension was reduced in the hospital in a few days by intensive use of eserine, then an iridencleisis was performed; a small hyphema was promptly absorbed, and the tension was 8 mm. Hg, 10 days after the operation. Undoubtedly, the cataract will have to be removed soon.

In summarizing this case it might be said that we have here a glaucoma capsulare developing over 10 years after the patient was first seen and operated on for glaucoma (capsular ?) of the fellow eye. For six years he had no suggestion of glaucoma of the right eye, and then only a slight increase in tension. He had had no symptoms until four years later, when he began to notice colored halos about lights, and a slight reduction in visual acuity. The fields were suggestive but less so than formerly. The anterior segment was apparently normal—no changes would have been found, had not, in spite of the tension, the pupil been dilated.

Slitlamp examination led to his immediate hospitalization and an operation. The slitlamp would have been of decidedly less use if the pupil had not been dilated. Miotics would have been administered if we had not wanted to use the slitlamp *after dilatation*. But with a tension already above normal only an adrenalin preparation would induce the dilatation necessary with the minimum danger of acute hypertension.

The slitlamp would be used more if it were more available. A *large* dark room is of great advantage, for several instruments can be instantly serviceable.

No general examination would be complete without a blood-pressure reading—systolic and diastolic—yet how often is it found abnormal? If it were taken only when some abnormality were suspected, how often would it be taken? But is ocular tension taken with the tonometer routinely or only when some abnormality is suspected? The conscientious comparison of tension taken with fingers and with the tonometer should lead, if the manual tension proves to be unreliable, to making *routine* tests with the tonometer.

Only rarely do patients object to ton-

ometry. Possibly the procedure has been presented in an unwise way; or they may have been hurt by having the tonometer used on a still sensitive cornea, or frightened unaccountably. It is rare now to encounter anyone who objects to anything that is done in the office; taking the tension before and after cycloplegia in all except the youngest children is routine. Even in children it is often wise to take repeated tensions.

A case illustrating this was recently published in full in the Journal of the American Medical Association (1938, v. 110, Jan. 1, p. 38). The patient was a young girl who had a number of symptoms suggestive of glaucoma, including apparently a high tension, considerably contracted fields, enlarged blind spots, and reduction of accommodation (hypercyclosis). After thorough anesthetization of the cornea no increase of tension occurred, even after the use of homatropine. In a general examination it was found that the patient was in need of the proper advice and attention coincident upon changes of puberty. Following this she had no more trouble, and the fields and blind spots returned to normal.

A patient with retinitis pigmentosa may develop glaucoma. Many patients develop glaucoma after successful cataract operations. The tonometer is almost as important to the opthalmologist as the thermometer is to the pediatrician. The technique of taking tension is important. Adequate anesthetization, the proper balancing of the tonometer and holding of the lids, and lack of resistance in the patient are essential.

Refraction is a division of ophthalmology in which it is almost impossible for any eye physician to change his habits radically. Refraction is largely done in routine fashion, and perhaps routine is slavishly followed instead of being treated as a servant. If there is only a slight change in sphere, cylinder, or axis, are new glasses blindly ordered or is evidence of trouble sought elsewhere? The eyes can often stand considerable maladjustment of glasses; otherwise folks—millions of them—would not stand for department-store fittings; or for the miserable frames and incorrectly ground lenses often given patients by careless opticians, especially in the cut-rate stores.

Dr. A. Duane had a system in his refraction that might be regarded as almost ideal and followed in general, if not in every detail: (1) A careful manifest refraction, in which ⅛ D. sphere and cylinder and 5-degree axis played a large part. (2) Measurement of accommodation of each eye alone and of the two eyes together. (3) Cycloplegia (homatropine except in children) every 10 minutes until the measurable accommodative range was .50 or .75 D. Then another careful manifest refraction. Then he would add a +1.00 D. sph. to this correction and send patient and assistant into the dark room to check. If the latter differed by ⅛ D. sphere or cylinder or 10-degree axis he would re-check at the trial case or recheck the retinoscopy. In this way he did not usually think it necessary to do a postcycloplegic examination.

At the Academy recently more has been reported about benzedrine-homatropine refraction. We have tried this in our office and like it in some respects. It does not fit into the office scheme we have worked out so well as does straight homatropine-cocaine or atropine refraction. We have also tried scopolamine refraction and abandoned it as being inapplicable in our office. It must be remembered that in the end the patient is the judge of the comfort or discomfort of glasses. If they are uncomfortable something is wrong.

On what percentage of patients are fields taken? On only those in whom there is a suspicion of pathological findings? Some years ago Dr. Emory Hill of Richmond stated that in his office he or his as-

sistant took on an average of three fields per day. Fifteen percent or more of his patients had had one or more fields taken. It will be very satisfactory for him to know 15 years from now that Mr. Smith had such and such a defect in December, 1937, and that the defect had not increased. Unless fields are taken now, the information will not be available 15 years hence. Of course, all glaucomatous suspects should have many field studies made, also all neurological patients. The more fields we take the more pathological conditions we will find, and the better we will find ourselves able to evaluate fields.

The technique of taking fields is not difficult to master, and can be taught to an assistant, especially if the assistant is intelligent and coöperative. Both perimeter and campimeter or tangent screen are so essential that one wonders how any intelligent ophthalmologist can get along without them. An inexpensive arc and an inexpensive curtain and targets which may be handmade are all the requisites. Some refinements are advantageous.

The photometer may yield a clue as to the functional ability of the retina. The function may be lowered by vitamin deficiency or other pathology—neuritis, glaucoma, vascular disease, and allied conditions. This test is very easily made by the Birch-Hirschfeld instrument made by the Zeiss Company.

Transillumination should be routine on certain cases—especially in all monocular glaucomas (but it is useless in heavily pigmented peoples such as dark negroes), also in every case of detachment, even in those with myopia or those with traumatic history. Here also the technique is exact—and the instrument should be adequate. Unfortunately, most transillumination is done in a careless way and with an inadequate instrument, such as the tip of the electric ophthalmoscope.

Let us return to the eyelids. No longer are the canaliculi slit up or probed indiscriminately, thanks to the repeated condemnations of Drs. Wilder, Beard, Hotz, the elder Gradle, and others. But have we not gone too far the other way? Do we examine the size and position of the puncta? If they are abnormal and are causing symptoms, do we routinely attempt treatment? Simple silver-nitrate or silver-albuminate treatment of the lids, dilating the puncta, irrigating the sacs, are techniques of which we do not make enough use. Also we are apt to forget that boric acid alone or in combination with other medication is very gratefully borne. Many of Dr. Wilder's old patients remember him as kindly for his boric camphor eye wash as for his glasses.

A thorough inspection of the eyelids is essential to a routine and complete ocular examination. One may find an eyelash in a lacrimal punctum; minute unpigmented hairs growing towards the eye; a double row of eyelashes. And are we too busy to take smears and cultures?

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ACUTE EPIDEMIC SUPERFICIAL PUNCTATE KERATITIS*

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Acute epidemic superficial punctate keratitis was first independently described in 1889 by Fuchs[1] and others, and since that time has, in its more usual aspects, been clinically recognized. Some writers prefer to designate it as a manifestation of disease and not as a specific disease entity. The clinical features in their various forms are still liable to extensive variations. This disease[2] has occurred in India[3, 4] a number of times in epidemic form. It has also been reported from Japan.[5] A search through the available literature reveals that but one epidemic has been reported in this country, that by Dr. Alfred Dean,[6] of Grand Rapids, Michigan, in 1930. This fact alone would lead one to conclude that in epidemic form it is a disease not frequently encountered.

The epidemic whose description follows herewith occurred at the Veterans Administration, San Fernando, California, in September and October, 1936. Many of the characteristics of the cases checked rather closely with those reported by other observers.[7] However, the predominant clinical findings in the various epidemics in different countries have shown a rather wide variation. We had but 16 cases, which, for statistical purposes, is not a large number. Clinically, all of our cases were ushered in with a violent conjunctivitis (unilateral in only one case), both ocular and palpebral conjunctivae being markedly reddened, swollen, and edematous, with about equal severity in each eye, in contrast to the later corneal symptoms which affected one eye to a greater degree than the other. Photophobia and lacrimation were very pronounced. Pain was not severe in the conjunctival stage, which lasted from 10 to 14 days and ran a rather definite course. At first, we thought we were dealing with a virulent form of conjunctivitis. This opinion, however, was short lived, for repeated smears and cultures made from material taken from conjunctival cul-de-sacs of all patients failed to reveal the presence of offending organisms.

Dimness of vision was not present until the later development of corneal symptoms, which in our series began with a haziness of the cornea. The lesions consisted of minute, opaque, grayish dots, involving, for the most part, the second layer of the cornea. Some may have extended into the deeper structures. The number of dots varied from 20 to 100, some being evenly distributed, but the majority showed a tendency to occur in a triangular aggregation (base down). This peculiar arrangement of the deposits may be explained by their mode of origin. They are conglomerations of cells held into masses by means of fibrin. Motion of the eyeball and gravity may have played a part in placing them in this position. With the aid of a slitlamp it was possible to make out very minute deposits forming a faint haze on the basal layers of the corneal epithelium. In our more severe cases, the cornea appeared rough and uneven. However, none of the corneas would stain with fluorescein.

The etiological factor of this disease is still very much in doubt. Most observers are inclined to associate the disease with

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minor infections, such as styes, marginal ulcers, dental-root and respiratory infections, not to mention such well-known offenders as chronic infected tonsils and chronic sinusitis.

It is difficult to understand why so few as 16 cases of this unusual eye condition would develop at one time instead of the manifestations usually associated with general or focal infections. Our cases developed in a few days following a 48-hour period of a hot desert wind. It is the writer's opinion that this epidemic had an allergic basis. Many observers have long recognized the fact that the eye is prone to develop disturbances of hypersensitivity.

Someone has attempted to rule out the air-borne theory as a causative factor on the grounds that such a widespread disease is rarely a binocular affection. In our series, however, just the opposite was true, for there was but one unilateral case. If this epidemic was due to a focal or a general infection, it would seem that constitutional and local treatment would not have failed to such an extent. A vitamin deficiency seems unlikely, as all patients did not eat at the same mess; some were on a high-vitamin diet.

Age and sex were not a factor; however, no children were among these patients. Those affected included two members of the staff; others were kitchen help, ward attendants, and patients. Some were on infirmary wards, others ambulatory; all were living on the hospital grounds. It was in no way contagious. Ambulatory patients complained of considerable lassitude. The blood picture was not affected. One year later, we find that in all cases there is still a chronic, mild to moderately severe conjunctivitis. In four of the cases there is a definite reduction of visual acuity in one or both eyes. Absorption of deposits is not complete in these cases; there also remains a slight haziness of the cornea.

Only one of our patients developed corneal ulcer. When it is considered that the cornea is not provided with blood vessels, but derives its nourishment through a system of lymph canals, the difficulties presented in the treatment of an ulcer on this diseased background, not found in the ordinary ulcer in this location, can be appreciated. Some observers believe that punctate keratitis can occur without iris involvement if the keratitis is at all severe. This the writer is inclined to doubt. Tension was not taken in these cases, because of the already roughened corneal epithelium.

Treatment: The remedies usually employed in the conjunctival stage were more or less ineffectual. Keeping the patient in a dark room proved most beneficial. Either hot or cold compresses brought some relief. As to eye drops, these were of no benefit. For too severe pain the instillation of pontocaine solution or the ointment is recommended. Cocaine is contraindicated in these cases, in view of the already diseased corneal epithelium.

Atropine, no doubt, would have proved highly beneficial if used earlier in the disease. In a conjunctivitis of this severity, an early engorgement of the iris vessels may occur, producing a spastic miosis which greatly inhibits the action of atropine. Consequently, we obtained only slight dilatation of the pupils, and that with difficulty. Our more severe cases were complicated with a low-grade iritis. The pupils in the earlier stages were contracted. In the later stages, dionin[8] was, perhaps, the most widely used drug. Due to its decidedly irritant effect on the conjunctiva, inducing an increased lymph flow into the corneal lymph channels, it is usually employed in no greater concentrations than 5 to 10 percent. The ointment may also be used. After the initial irritant symptoms have passed, it exerts a marked anesthetic effect.

Quinine bisulphate is one of the more recent remedies. It does not possess the anesthetic effect of dionin. No one has yet come forward with a treatment that will definitely hasten the absorption of the deposits. They have been known to remain for a period of two years or longer, in some instances leaving permanent damage. Our treatment for the most part was symptomatic. When the varying clinical aspects of this condition are taken into consideration, it is easy to appreciate the treatment problem that confronted us.

Summary

The causative factors in this disease are very much in doubt. Most authors point out that it is usually associated with focal or general infections. If this were true, it would seem that since all adults have enough infection, either focal or general, stored in their systems, an attack could be precipitated at almost any time, and would not necessarily appear in epidemic form. But if the case were sporadic, the cause would still be undetermined.

In the early stages, this is not an easy disease to recognize. Many of the problems that were encountered by the early investigators half a century ago are yet without satisfactory solution. Dean,[6] oddly enough, presented a depression angle as a possible causative factor in his cases. After reviewing the available literature, also the high lights of our own epidemic, one is forced to conclude there still remains a lack of unanimity of opinion in regard to this unusual eye condition.

Veterans' Administration.

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NOTES, CASES, INSTRUMENTS

PRIMARY EPIBULBAR PRICKLE-CELL EPITHELIOMA*

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The successful treatment, by surgery and radium irradiation, of an epibulbar prickle-cell epithelioma is herewith reported.

J. S., a white male, aged 68 years, was seen by us on May 17, 1935. In March

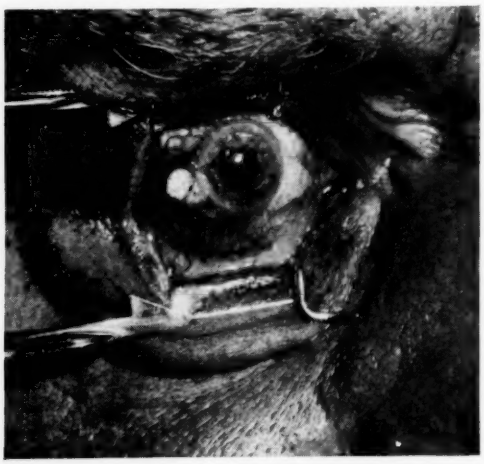

Fig. 1 (Binkley and Motto). Primary epibulbar prickle-cell epithelioma.

of that year he had the sensation of a foreign body in his right eye and some time later he saw a small yellowish-white spot on the eyeball. There was no pain, no photophobia, nor lacrimation; only a slight discomfort. There was no history of direct trauma. He had worked in a stone quarry for 20 years, then as a railroad laborer for 10 years.

On the temporal side of the cornea of the right eye at the limbus was a sharply defined, raised pearly white, ovoid tumor measuring $5 \times 6 \times 3$ mm. It extended from the 7- to the 9-o'clock position at the limbus. The conjunctiva surrounding the mass was highly vascularized. The mass itself was hard and firmly attached to the structures beneath. The top of the tumor was denuded of its epithelium. The pupil reacted sluggishly to light and to accommodation. Intraocular examination was negative. Vision, O.D., was 6/20; O.S., 6/20. There were no enlarged preauricular lymph nodes. The blood Wassermann and Kline tests were negative.

At operation, the tumor separated easily from the sclera, but was so firmly attached to the cornea that sharp dissection was necessary. After removal of all visible tumor tissue, the base was cauterized and the conjunctival defect closed with a sliding flap which was sutured with silk.

Microscopic examination: On one side of the section could be seen a fragment of normal conjunctiva. In the remaining portion there was a nodular tumor composed of irregular masses of atypical, but well-differentiated prickle cells. These masses merged into each other and formed the picture of an infiltrating proliferative process, unquestionably malignant. The interstices between these cell masses were occupied by a loose fibrous stroma in which were many lymphocytes. Within the tumor tissue there were epidermal pearls and numerous mitoses.

Method of radium irradiation: Six days after operation, the biopsy having confirmed the clinical diagnosis, the eyelids were closed by suture. Two 1-mg. low-intensity radium needles were inserted, one through each eyelid in opposite directions and were tied *in situ*.**

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** The specifications of these needles are: length 27 mm., diameter 1.65 mm., wall thickness of platinum-iridium 0.5 mm. A central

The needles remained for seven days in the eyelids, separated from the site of the epithelioma by the tarsus and conjunctiva. The total dosage given was 336 mg. hours.

The patient has now been followed for more than two years and thus far has shown no local ill effects from the use of radium. His vision remains as it was before the operation; namely, 6/20. When last seen there was a slight scar on the cornea and no evidence of recurrence of the malignant process.

That even a larger dose of radium will not harm the eyeball is shown by a case of round-cell sarcoma of the sclera, extending onto the cornea of the left eye, which we treated in November, 1933. In this case five 1-mg. radium-platinum-iridium needles were used. Four were inserted through the lids in the manner described above and one was placed into the tumor tissue between the eyeball and the orbital wall. In five days the total dosage became 600 mg. hours. To date (September, 1937) there has been no evidence of damage to the normal tissues of the eye.

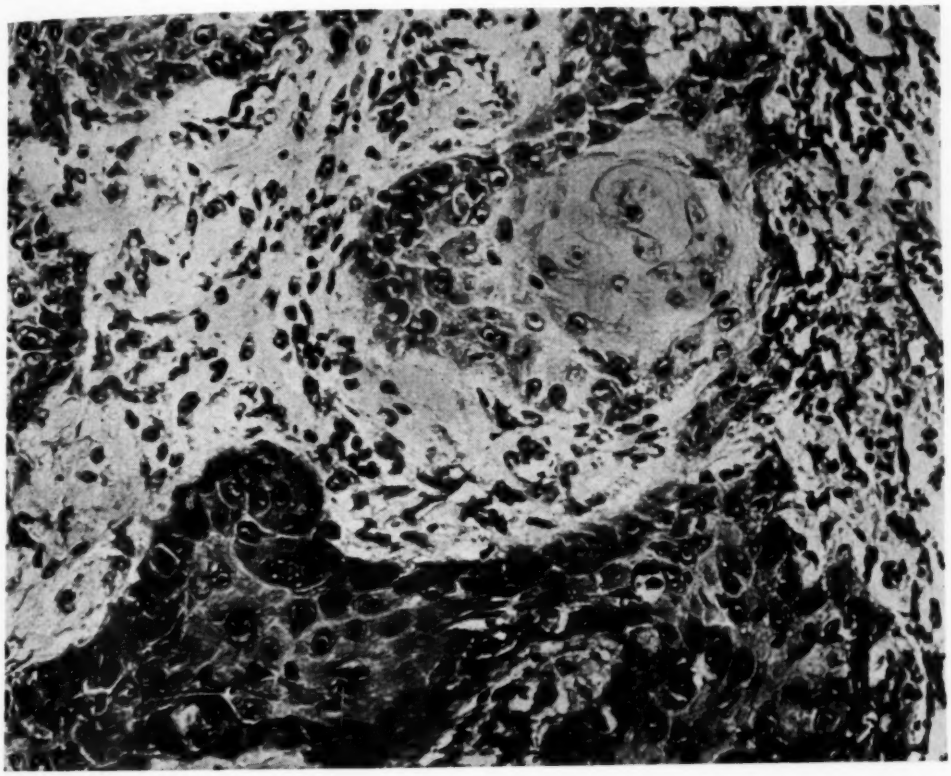

Fig. 2 (Binkley and Motto). High-power photomicrograph showing a well-differentiated prickle-cell epithelioma. In the upper portion a typical pearl can be seen.

Comment. Lane[1] states that the eye tolerates radium well. In her review of the literature to 1924, she found that bad results occurred in only four out of 500 patients.

cavity 15 mm. in length contains the equivalent of 1 mg. of radium element. Long gamma rays and 99 percent of the beta rays are absorbed by the platinum-iridium wall.

Radenbaugh[2] has shown that unfiltered radium can be used for superficial lesions, and he reserves heavily filtered radium or X rays for deep-seated lesions. His technique in corneal, scleral, and superficial lesions of the lids is as follows: "Unfiltered radium sulphate, contained in a glass tube, is held in place over the lesion. The position of the tube is observed during treatment. Radium is used in the amount of 25 to 50 mg. The time ranges between two to ten minutes, being varied as to the thickness of the tumor. An intense superficial reaction with a minimum of depth dose is sought." In his four case reports he records disappearance of new growths, but does not give data on visual acuity.

Laborde[3] reported the complete disappearance of 50 out of 56 lid epitheliomas. She thus describes her technique: "Needles containing 2 mg. of radium element filtered by 0.5 mm. of platinum are introduced within the carcinomatous tissue and left *in situ* for a period of three to seven days, depending on the size of the lesion."

Cochran and Robinson[4] used radium immediately after healing of the operative wounds in their case of multiple epidermoid carcinoma of the eye and lid and obtained an excellent cosmetic result. At the time of their report, three months after radium therapy, examination disclosed no damage to the cornea or lens, no conjunctivitis and no recurrence. They did not give the technique of the application of the radium.

In our case of epibulbar prickle-cell epithelioma, gamma rays of radium caused the complete disappearance of the tumor without causing damage to the normal tissues of the eyeball. In the hands of experienced operators, radium with any amount of filtration has been found to be an effective and safe means of treating benign and malignant processes about the eye.

650 Rose Building.

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A TREATMENT FOR CHRONIC DACRYOCYSTITIS

REPORT OF THREE OPERATIONS BY A MODIFIED NEESE METHOD

PAUL SOUTHGATE, M.D.

Long Beach, California

When one turns to the literature for the treatment of chronic dacryocystitis he finds so many operations advocated that he might wonder if chronic dacryocystitis can be cured by any of the many different procedures or whether, like syphilis, it is a disease that may not respond satisfactorily to any treatment yet discovered. A little experience teaches the beginner that the latter condition is the true one.

Hofrat Fuchs said, "Chronic dacryocystitis is an inflammation of the lacrimal sac due to impeded outflow and consequent stagnation of the tears." A preliminary report of what the author thinks is a better operative treatment for this condition is here submitted.

Most of the present-day methods of handling this problem are well known.

Perhaps the simplest procedure recommended is teaching the patient to obstruct the canaliculi by pressure with the thumb nail, at the same time making pressure on the sac. This in some cases will empty the contents of the sac into the inferior meatus and in that way keep the eye clean for a few hours or longer. A small number of cases will clear up with probing. Infants, of course, regularly respond to probing.

We have all heard of the procedure of placing an indwelling tube in the lacrimal duct to extend from the sac to the inferior meatus. Dr. Pratt of Minneapolis has long favored this procedure. Perhaps the most universally used procedure is the removal of the sac. Several different techniques are used to obtain this result; also Gifford's cauterization with trichloracetic acid is another way of destroying the sac. Then, there are the dacryocystorhinostomies, and the names of Toti, West, Poliak, Dupuy-Dutemps, Mosher, and others come to mind.

There can be no doubt that many patients have been made comfortable by each of these procedures or modifications of them. But the author felt that none of them was as satisfactory as it should be. Either the results were poor, compromises between health and the original disease, or the operative procedure seemed so difficult as to make it unsatisfactory for the average ophthalmologist, who may not be called upon to treat this condition oftener than two or three times a year. So he started looking for a procedure that would, first, relieve the patient of the symptoms of chronic dacryocystitis; second, as far as possible restore the function of the lacrimal apparatus. It seemed as though these ends should be within the reach of an easy operation, since the nose and the sac are so close together and both easily accessible.

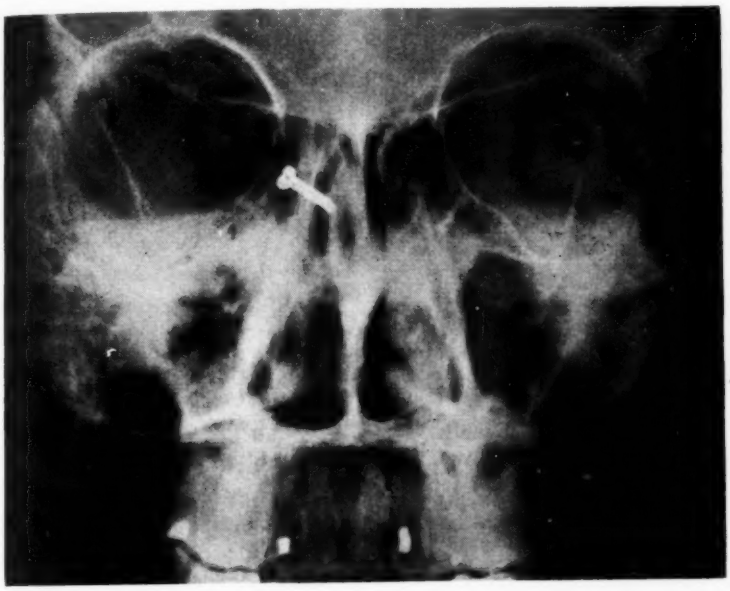

Fig. 1 (Southgate). Roentgenogram of tube in place one year after operation.

The author came upon a procedure that answered these three points admirably. Its originator, so far as the present writer has been able to discover, was Dr. O. R.

Neese, United States Navy, stationed at Long Beach, California, in January, 1937. He assisted the author with the first of his operations employing this method. Dr. Neese had used it on seven patients, with very satisfactory results in six. The one who failed to respond satisfactorily had had the lower canaliculus slit previous to his coming to Dr. Neese.

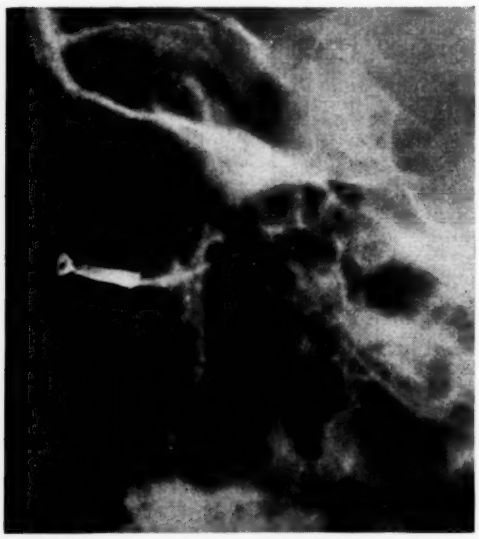

Fig. 2 (Southgate). Lateral view of the same patient.

The author believes that those who try this operation will also like it. It is simple and the results are gratifying.

The theory of the procedure is that of the dacryocystorhinostomies; that is, to drain the lacrimal sac directly into the upper nasal cavity. But the technique is simpler than any the author has found in the literature. After anesthetizing the area around the sac by injecting 4 percent novocaine-adrenalin, and the adjacent nasal area by the application of a cocaine-adrenalin pledget of cotton, the lumen of the sac is exposed with an incision similar to but smaller than that used in extirpation of the sac. A fine hemostat is then forced through the sac wall, through the paperlike lacrimal bone, and into the nasal cavity. A thin short metal tube is put into this opening, pointing downward into the nose. The skin and sac wall are closed with sutures.

The tube that the author now uses is 15 mm. long by 2 or 3 mm. in diameter. It is made of very thin metal, either of stainless steel or gold, and fenestrated by three holes in the shaft. A flange of gold solder is attached to the sac-end to keep the tube in place. The tubing can be obtained from an orthodontist, and the tubes made by the dental laboratory.

Occasionally it is necessary to straighten a deflected septum or remove the anterior tip of a large middle turbinate before the tube can be properly inserted. These are difficult problems in dealing with children.

The tube may be left in place permanently or it may be removed in 2 or 3 months. Removal through the nose under either local or gas anesthesia is easily effected. By that time a fistula has been formed and this functions as well as the tube.

Further details of procedure would include filling the sac with methylene blue to help identify it when it is opened. A Bowman probe placed in the lower canaliculus, projecting into the sac, helps in identifying the sac. To verify the fact that the sac has been opened, a probe may be passed down into the nose, where it can be tapped in the inferior meatus with a metal instrument.

One of the most desirable features that any operation can have is that it may be undone at will—which is true in this case. The tube can be removed and any of the generally accepted procedures still be performed if desired.

Dr. Paul Arganaraz of Buenos Aires reported an operation in 1921, that is similar to this. In this operation, he slit the lower canaliculus, then with a fenestrated tube on a heavy stilette, passed

the stilette and tube through the lower canaliculus and through the wall of the sac into the nose. Withdrawing the stilette, he left the tube extending through the wall of the sac. This appears to be an admirable procedure, being at once simple and effective, yet the author does not like the mutilation of the canaliculus.

Case reports

Case 1. A 35-year-old fireman had tearing of the right eye for four months, with two attacks of acute dacryocystitis accompanied by tremendous swelling and pain. Probing between attacks did not relieve the condition. Pus could always be expressed from the puncta. The anterior tip of the right middle turbinate was large, and was therefore removed. Two weeks later a tube was put in place. This was before the idea of fenestrating the tube occurred to me. A little trouble was experienced in keeping the end of the tube in the nose open, but after removal of a few granulations the eye remained dry and comfortable. The patient says that about once a month the tube gets stopped up. He opens it by holding his nose with his thumb and finger and forcing air into his nose. After this, the eye is perfectly comfortable.

Case 2. Mexican boy, aged 14 years, complained of a continuous profuse purulent discharge in the left eye for eight years. The anterior tip of the middle turbinate was removed. Two weeks later a tube was put in place. In a week, the offending eye was as dry as its fellow, and the pus had entirely disappeared. In two weeks the wound was healed. Six months later the patient was still symptom free.

Case 3. A nine-year-old boy had had tearing all his life in the right eye. There was no pus. The author was unable to irrigate through either canaliculus. He could not satisfy himself that the canaliculi were patent. It was with some misgiving that he decided to put a tube into this sac, in the hope it would stop the tearing. In two weeks after the tube was inserted, there was no tearing, nor was there any for two months, but the wound was suppurating. The tube was removed and replaced, directed more downwardly. Now the wound is well healed and the eye is dry. The canaliculi were, of course, patent or this operation would not have given relief.

Summary

This is the preliminary report of what the author feels to be a better operation for the treatment of chronic dacryocystitis. The theory of the procedure is to drain the lacrimal sac directly into the upper nasal cavity by putting a small stainless-steel or gold tube through the lacrimal bone into the nose. The end of the tube is held in the sac by a small flange. This tube is left in place indefinitely or is removed in 2 or 3 months. Removal is by way of the nose. A fistula will have been formed which permits the sac to drain into the nose. The technique is simple. The lumen of the sac is exposed. A small blunt instrument is forced through the sac wall, through the thin lacrimal bone, into the upper nasal cavity. The tube is put into this opening directed downward into the nose. The wound is closed, leaving the tube in the sac, pointing downward into the nose. The operation can be undone at any time, and any of the standard procedures used without additional complications.

Dr. Neese, the first to use this procedure, reported seven cases, six with good results. In the author's series of three cases, all responded very satisfactorily.

The author wishes to express his appreciation to Drs. Heylmun and Mayfield for the excellent X-ray illustrations.

704 Professional Building

SOCIETY PROCEEDINGS

Edited by Dr. H. Rommel Hildreth

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Section of ophthalmology

November 12, 1937

Dr. Walter E. Camp, *president*

The mechanics of iris prolapse after cataract extraction

Dr. Anderson C. Hilding of Duluth, said that it had been his privilege to work one season with Sir Henry Holland in his eye clinic at Shikarpur, Sind, India. While there he had had an unusual opportunity to observe directly the mechanics of iris prolapse. His discussion was limited to prolapse caused by escape of aqueous through operative incisions at or near the limbus and would not deal with prolapse due to loss of vitreous or other contents of the eye.

There were numerous patients coming to the clinic at Shikarpur daily, seeking help for poor vision due to corneal leucomata, sequelae of trachoma, and various types of ulcer, including smallpox. An optical iridectomy was performed on a great number of these patients. One routine step in this operation was to produce iris prolapse purposely. After making a limbal incision with a Graefe knife, the knife was turned, and with the end of the handle a push was made against the opposite side of the eye just posterior to the limbus. As a result, the iris would promptly herniate.

The prolapse would not occur excepting under certain conditions, the various steps of which seemed to be about as follows: (1) as the incision is made, collapse of the anterior chamber; (2) formation of a water-tight seal between the iris and the cornea as the iris and lens push forward; (3) imprisonment of the aqueous in the posterior chamber when escape through the pupil is cut off; (4) sliding of the iris upon the posterior surface of the cornea toward the incision; (5) ballooning of the iris as it enters the wound; (6) collapse of the balloon as the pupillary margin of the iris reaches the wound liberating the enclosed aqueous. The prolapsed iris remains incarcerated between the lips of the wound.

If these observations were accurately made, it follows that three factors are essential for the production of prolapse: (1) sudden loss of aqueous from the anterior chamber; (2) imprisonment of aqueous in the posterior chamber by a seal formed by contact of the iris against the posterior corneal surface; (3) continued pressure, which forces this fluid through the wound ballooning the iris before it. If any of these factors can be controlled, prolapse will not occur.

Now to apply this to cataract surgery. The lens, of course, is no longer in place after the operation, but it seems that the vitreous body acts similarly in pushing the iris against the cornea. Unless the chambers have refilled after operation there can be no prolapse, and the chambers do not refill until the lips of the wound are sealed and are watertight. Consequently the extreme care used in handling the patient's head in applying the dressing and in removing him from the operating table is not essential. The Viennese practice of allowing a patient to walk from the operating room to his bed is perfectly rational and not dangerous from this standpoint. There is much more danger on the day following the operation, when the intraocular tension has returned to normal and when the wound is

closed by a fragile fibrinous seal which may suddenly give way from any slight force applied to it.

Many procedures have been devised to keep the lips of the wound together, among them various types of conjunctival flaps. Unfortunately, the conjunctiva is so distensible that the wound may open and prolapse may occur subconjunctivally. This is common experience. Corneoscleral sutures are very effective in holding the wound closed at the point of the suture, but one or two sutures are insufficient to keep it tightly closed throughout its length. It is not uncommon to see a wound open near the angles, even when a suture at the 12-o'clock position is holding well. Enough sutures (four or five) might be used to avoid any possibility of the wound opening, but owing to the difficulty of inserting them, it is not very practical to use so many.

Iridectomies and iridotomies are used to avoid the second factor; namely, imprisonment of the aqueous in the posterior chamber. The standard complete iridectomy at the 12-o'clock position, extending from pupillary margin to the root, is effective only if the wound should give way in the neighborhood of the vertical meridian, but if the lips of the wound should part at one side, the underlying intact iris would cover the defect and be forced out by the aqueous behind it. These prolapses of one column or the other or both are also common experience.

Referring again to the experiences in India, a few trials on the patients who were to have full, optical iridectomies demonstrated the effectiveness of a small iridectomy. It is possible to make a short limbal incision and then quickly and gently to make a tiny peripheral iridectomy without losing much of the fluid from the posterior chamber. After doing this the iris would not prolapse when pressure was made, even though the aqueous squirted through the iridectomy in a little stream several inches long.

It follows, of course, that the iridectomy has to coincide with the incision or the aqueous could not escape. If the iridectomy were placed central to the incision, the iris would slide toward the incision until the hole entered the wound and the aqueous escaped through it. One iridectomy alone, however, is not enough to control the second factor with certainty—in the case of a long cataract incision. Three alone are not enough either, for he had seen a prolapse occur at least once when three iridectomies had been used. One or two sclerocorneal sutures alone will not with certainty prevent the incision from opening and leaking. But a combination of the two sutures and three iridectomies affords a practical method which seems to prevent iris prolapse with reasonable certainty. The iridectomies are placed between and on each side of the sutures.

Since returning from India, his standard operative procedure is as follows: two sclerocorneal sutures radially placed at the 10:30- and 1:30-o'clock positions; incision within the loops at the limbus without conjunctival flap; three tiny peripheral iridectomies at the 10-, 12-, and 2-o'clock positions; intracapsular removal of the lens through a round pupil.

Thus far, there had been no iris prolapse in a single case in which the stitches were in place at the end of the operation. The sclerocorneal sutures are put in before the incision is made in a manner similar to that used by Verhoeff four or five years ago, and do not penetrate into the anterior chamber.

The effectiveness of the method is further illustrated by several eyes in which the anterior chamber reformed only to collapse again, a day or two later. In all of these instances the iris remained in good position with a round central pupil.

The series of cases in which this method has been used is unfortunately too small

alone to establish the value of any method. It consists of only 33 operations, omitting one in which both stitches were accidentally cut. In none was there any sign of prolapse or visible incarceration. Of these 33, 31 healed with round central pupils. In one of the remaining two, the pupil was drawn upward somewhat, but no incarceration was visible externally. In the other, the pupil was oval in the vertical direction apparently because the pupillary margin at the 12-o'clock position had been folded backward between the ciliary body and the vitreous.

In addition to the prevention of the prolapse, this method has very distinct advantages in the postoperative care. It becomes unnecessary for the patient to lie so exceedingly still in bed. A cough, sneeze, vomiting attack, or straining at stool does not carry the danger with it that it otherwise does. The patients in this series have been allowed to sit up in bed the day after the operation, and in a chair on the second postoperative day. There really seems to be no reason why they could not sit up immediately if they so desired. They have been given a full diet copied as nearly as possible after that which they ordinarily eat at home, instead of the scanty liquid diet often prescribed. When they have felt uncomfortable from constipation, they have been given enemata without hesitation. The result has been that with reasonable freedom of action, their accustomed diet, and lack of constipation, these elderly patients have gone through the experience of cataract operation much more happily and with less distress and untoward after-effects than did our patients formerly.

Discussion. Dr. R. O. Leavenworth, St. Paul, said that he makes an incision with a bridge continued above, and the lens is delivered under this bridge. Prolapse under this bridge has not occurred, but there is always danger at the angles. He thought that the most frequent location of a prolapse is at the temporal angle, possibly because this location is more exposed and the bandage less secure than it is at the nasal angle, which is next in frequency. He found that the nasal angle was apt to prolapse when he made a single, peripheral iridectomy on the temporal side, and so concluded that the proper procedure was to make a double iridectomy; that is, both temporally and nasally. Both Dr. Lewis and he had done this for a number of years. He did not recall a single prolapse.

Dr. Charles N. Spratt, Minneapolis, said that prolapse of the iris can be avoided if one performs an iridectomy, especially in patients 70 years of age. For many years he had followed the method of Chandler, who made a small buttonhole in the iris at the base. In making the incision in the pocket-flap method, a method which he had long followed, a prolapse of the iris is not of serious consequence, as the tissue is covered by a strong layer of conjunctiva. The tendency toward late infections is not more likely than in the modern operation for glaucoma (iridotasis).

He has his patients sit up after the operation and has them out of bed the following day, as he thinks there is less disposition toward prolapse if the iris is in the vertical position than when the patient lies down and the iris is horizontal.

George McGeary,
Secretary.

ROYAL SOCIETY OF MEDICINE, LONDON

SECTION OF OPHTHALMOLOGY

November 12, 1937

MR. W. H. MCMULLEN, *president*

PLASMOCYTOMA OF THE LACRIMAL GLAND

MR. S. T. PARKER, of King's Lynn, commented on the rarity of the condi-

tion, and explained that his paper was founded upon the following case. The patient was a man aged 66 years, who sought advice because he and those about him noticed that his left eye had appeared to be gradually closing for the previous ten months. When the man was examined there was seen to be ptosis and some undue prominence in the outer half of the supraocular sulcus. The marginal portion only of the upper eyelid was capable of voluntary movement, and that only slight. Digital examination revealed a firm, somewhat lobulated subcutaneous swelling which seemed to be extending from the lacrimal-gland fossa. All the ocular movements were free, there was no diplopia, vision was 6/6 unaided, and fundi and media appeared to be normal. The most likely diagnosis seemed to be tumor of the lacrimal gland, and so it was found to be at operation a few days later. The lacrimal gland, which was enlarged to about two-and-one-half times its normal size, was removed without great difficulty. Its color was grayish brown, it was slightly lobulated, firm in consistency, and encapsulated. At one point the capsule was thin, and appeared to be torn. The bony wall of the orbit in its upper part seemed to be normal, and a portion of gland seemed to have been left behind. The recovery of the patient was uneventful.

Microscopically, the specimen was found to be a very cellular nodule of tissue, and there was a definite attempt at encapsulation by fibrous connective tissue. Fibrous tissue trabecula, many of them very thick and solid, were seen to enter the substance of the nodule from this capsule, and, intersecting in the substance, to divide it up into lobules. Many well-formed blood vessels were seen to accompany these septa, but very few were seen in or amongst the actual masses of tumor cells. No areas of degeneration or necrosis were seen. The cells were indistinguishable from plasma cells, and had undergone slight distortion as a result of fixation, but were, roughly, oval or circular. The cell cytoplasm appeared to be amorphous. In most of the nuclei one or two nucleoli were to be seen. Mitotic figures were very scarce. The tumor beneath was plasmocytoma.

No sign of recurrence was detected for six months after the operation, and the patient resumed his normal life as a farmer. But gradually the inner half of the supraocular sulcus became obliterated by a second swelling, of similar size and consistency. After a year another new growth, slightly less in size than the first, was removed. It was adherent to the frontal bone, and there was some erosion of the floor of the frontal sinus. After the mass was removed, the surrounding area was cauterized freely by means of diathermy. Though recovery from this was good, the patient suffered from troublesome diplopia, due to the damage which had been caused to the superior-oblique muscle. As a number of observers had recorded good results from radium, this was tried six weeks after the second operation, and no further recurrence was noticed until eleven months had elapsed. Last July a tumor as large as that first observed was seen, and radium was again used, the needles this time being inserted more deeply. So far, there had been no further recurrence. The rest of the skull, long bones, spine, ribs, and sternum appeared to be normal. The Wassermann test was negative, as also were the urine tests, especially the Bence Jones albumose test. The blood was normal.

In the past, the term "plasmocytoma" has been employed to denote any form of tumor, either neoplastic or inflammatory, which is composed of plasma cells. The distinctive features of the plasma

cell, as seen under the microscope, were as follows: It was a large cell—that is, up to three times the size of a lymphocyte—and was either oval or polyhedral in shape. The cytoplasm was clear, and seemed to take more of the stain peripherally. The nucleus was eccentrically placed, with deep basophilic staining of its chromatin content, radiating in cartwheel form and condensed beneath the nuclear membrane. The size of the nucleus varied. A clear crescentic perinuclear zone in the cytoplasm could be definitely demonstrated by staining with hematoxylin.

The origin of the plasma cell is unknown. Many are of the opinion that it arises from a lymphocyte. Another theory is that it originates from fibroblasts arising in the endothelial lining of the blood vessels. The condition is rare in females. There are medullary and extramedullary forms. Twelve cases have been described, in which there was, on the average, 20 percent of plasma cells in the differential white count. In all of them, the high percentage of these cells was associated with diffuse infiltration in various parts of the bone marrow of the skeletal system, due to plasmocytoma.

The fact that some cases were associated with positive evidence of syphilis or tuberculosis, and also because plasma cells have been found in chronic inflammatory conditions, has induced some observers to consider these tumors to be of inflammatory origin.

Any kind of neoplasm of the lacrimal gland is a comparative rarity, but there is a possibility that some neoplasms described as lymphosarcomata were of this nature. Present knowledge of the histopathology of this condition, so far as it is related to the lacrimal gland, does not support the theory that plasmocytomata are of lymphocytic origin, but are, more likely, a type of endotheliomata.

British ophthalmology in the 16th and 17th centuries

Mr. Arnold Sorsby read a profusely illustrated paper on this subject.

Defective movements of the left eye

Mr. N. Ridley (for Mr. Affleck Greeves) presented a boy aged seven years, who was seen in the out-patient department eight months previously, because of having struck his eye on a door handle four days before. Since that accident he had had double vision, one image being above the other. After the event he vomited and had severe headache, but did not become unconscious. Vision in this eye was 6/9, that of the right eye 6/6. There was an absence of upward, and marked limitation of downward movement. Lateral movements were associated with a jerky movement, but it was not true nystagmus. Dr. Purdon Martin, neurologist, considered the condition to be due to a small hemorrhage at the apex of the orbit. No fracture was evident from the skiagram. In the last eight months the movements had become almost normal.

Deep stain of cornea: argyrosis from protargol

Mr. Frank Juler said the patient was an engineer aged 24 years. A toy pistol had exploded in his face in August, 1936, and he received multiple foreign bodies in both eyes. Protargol was used, in 2-percent drops, from November last year until last September, twice daily for both eyes. A fortnight ago vision was 6/5 partly in both eyes, and the eyes were now quiescent, except for a slight conjunctivitis. There was definite silver staining of the conjunctiva and of the

caruncle. There was a metallic fragment, deep in the 4-o'clock position, which had a glistening, yellow, rusty appearance. In an arc around it was a definite opacity, confined to the posterior layer of closely packed points. These showed a diffuse deep-blue color, which was most marked in the parts of the half-circle nearest the limbus. The question which arose was whether the blue color came from the foreign body, or a silver staining associated with superficial argyrosis. There were cases in which argyrosis had involved Descemet's membrane, causing a blue staining, more or less diffuse.

Melanotic sarcoma of limbus treated by excision followed by radium therapy

Mr. E. Keith Lyle presented a man, aged 60 years, who was seen at the hospital last April. The history was that fifty years ago the right eye was splashed with hot fat. This left an opacity on the white of the eye which gradually spread over the front of the eye, and in the form of a film, and interfered with vision; in the last two years it had become larger. On examining this right eye there was visible a large, raised, darkly pigmented plaque, extending over the outer half of the cornea, apparently originating from the limbus in the 9-o'clock position. There were numerous distending blood vessels running into the growth in its lower part. The pupil was active, the tension normal, and fundus and media were normal. The left eye was normal in every respect. Last May the growth was excised: it had been stripped off the cornea easily, but was more adherent in the limbal region. The conjunctiva over the growth in this region was also excised. At the Radium Institute, last June, he was given a surface application of radium, and in September a similar treatment. Microscopic section of the growth showed it to be melanotic sarcoma of the limbus arising from nevus cells. It was now proposed to administer one more application of radium.

Detachment of the internal limiting membrane of the retina

Mr. T. G. Fenton said the patient was a woman aged 23 years. In February, 1937, she had an attack of acute juxtapapillary chorioretinitis, for which no extraocular cause could be found. The condition had now reached a quiescent stage. There was an atrophic area of retina above and on the temporal side of the optic disc, with a corresponding wedge-shaped defect in the lower nasal visual field. The internal limiting membrane of the retina had become detached and lay in the vitreous close to the posterior surface of the lens, appearing as a thin transparent membrane with a round perforation representing the deficiency of this membrane at the optic disc.

Discussion. Dr. A. J. Ballantyne (Glasgow) said it was difficult to understand the internal limiting membrane coming forward, as this did, in a comparatively healthy vitreous. On focusing the ophthalmoscope upon the summit of it there was no surface of reflex, but there was the usual retinal surface reflex which was supposed to come from the anterior limiting membrane.

Mr. Eugene Wolff said it was what was usually described as a detachment of the hyaloid. He had seen, in pathological conditions, the membrane immediately behind the lens.

Mr. Ransom Pickard said his difficulty was in accepting it as the internal limiting membrane as, allowing for the hole corresponding to the disc, the membrane did not appear so uniform as would be expected. He thought that if the acute condition was a parachoroidal inflammation

there would have been vitreous opacities.

FILARIA BANCROFTI IN THE INTERIOR OF THE EYE

MR. W. H. MCMULLEN presented an Indian student, aged 25 years, who was first seen on September 8th last on account of having had inflammation in the left eye for six days. At the time he was being treated by means of X rays for spondylitis, from which he had suffered, on and off, since he was ten years old. No definite cause for that condition had been found. A year previously he had had inflammation of the left eye, which was diagnosed as iritis and which lasted 14 days. When seen by the speaker the eye was much injected and the aqueous slightly cloudy, with many floating particles. The pupil dilated well with atropine. The patient had intense pain, and treatment with leeches was ineffective. During examination with the slitlamp there suddenly came into view, in the aqueous, a minute, worm-like object, actively motile, very thin. After a few seconds it disappeared. Last month the signs of inflammation had almost subsided, but the slitlamp again showed a nematode worm. Colonel Wright also obtained a view of the worm. Admitted into the Hospital for Tropical Diseases, Dr. Cruickshank there found Microphilaria bancrofti in the night blood in fair numbers. The filaria skintest was negative.

Discussion. Mr. T. G. Fenton spoke of having had a similar experience, the patient being a West African. He had seen a worm three fourths of an inch long wriggling about just above the limbus, under the conjunctiva. After an instillation of cocaine, only the tail of the worm could be seen. On quickly cutting down on to the conjunctiva the worm was caught by the tail and extracted. Cocaine caused it to move very quickly.

Mr. T. Harrison Butler spoke of a case of Loa loa in the eye which he published, the patient being a doctor from the west of Africa. The patient had advised against the use of cocaine, as it drove the worm away.

NEW YORK EYE AND EAR INFIRMARY

CLINICAL AND PATHOLOGICAL CONFERENCE

November 22, 1937

DR. ISAAC HARTSHORNE, *chairman*

EXOPHTHALMOS AND HIGH MYOPIA

DR. D. C. SAVAGE presented a case of a 45-year-old woman who had been seen by Dr. Loren Guy, with a diagnosis of exophthalmos O.S., and high myopia. Vision O.D. was the ability to count fingers at three feet, with correction, 20/200; O.S. 15/200, with correction, 20/70. The protrusion of the eye began five weeks ago. The patient had some pain in the region of the orbit. The reading on the exophthalmometer was O.D. 20, O.S. 25; the movement of the left eye was restricted. The blood count was negative; the Wassermann reaction also negative. X rays were taken of the skull and sinuses which showed a decalcification in the floor of the frontal sinus. There was herniation of orbital fat through the tarsal orbital fascia.

Discussion. Dr. Brittain F. Payne questioned how this case should be handled; whether a biopsy, or an operation should be performed.

Dr. Samuel P. Oast said that he thought it was a hernia of orbital fat breaking through the tarsal orbital fascia. He did not think there was any special need to do anything about it, unless it interfered with the movement of the eye.

Dr. Isaac Hartshorne added that a re-

cent operation had been devised for this condition.

Dr. Nathan Berger said he had had a similar case three years ago. A woman, who was a cardiac and nephritic patient, and who refused surgical interference, showed by biopsy the condition to be a lymphoma. Six months ago Dr. Berger saw her again, and the growth involved the entire cornea and overlapped so that vision was impaired. Surgical interference was not advisable because of her general condition. X-ray and radium treatments were advised, and two weeks later the mass had receded and the cornea was free.

Complete detachment of the retina

Dr. Truman L. Boyles presented the case of a man, aged 35 years, who was first seen in June, 1937. Vision was 20/20 O.D.; O.S. the ability to detect hand movements, with complete detachment of the retina. He also had nephritis. His condition has progressed until now he has light perception O.D.; hand-movement detection O.S. Dr. Boyles questioned the advisability of operating for the detachment in the left eye. He added that the patient has been in the hospital for three weeks under strict medical supervision, but has not improved.

Discussion. Dr. Raymond E. Meek said that because of posterior cataractous changes, and because the pupil was not wide enough, he could not make a definite diagnosis. He did not think that surgical interference should be attempted at this time.

Dr. Samuel Oast thought this might be a case of Coats's disease, since he saw some hemorrhages.

Dr. D. Blair Sulouff suggested that the hemorrhages might be due to diabetic retinitis.

Calcification aneurysm of the internal carotid

Dr. Nathan Berger presented the case of a man, 54 years old, who had come under his observation in June, 1937. The patient had loss of sight O.S. for one year. The Wassermann reaction was negative; the blood pressure 114/68. A diagnosis of calcification aneurysm of the internal carotid was made by roentgenogram, which showed a distinct ring in the region of the optic nerve; no enlargement of veins was noted.

Alcohol and tobacco amblyopia

Dr. Frank Carroll of Columbia Medical Center said that his experience was limited to between 125 and 150 cases. He pointed out that this condition often occurs in people who have been smoking and drinking for a long period of time. The amount of reduction in vision varies considerably—that is, it may be from 20/20 or 20/30, to counting fingers—a blurring sensation is apparent; visual acuity is reduced, and the condition occurs in both eyes. Generally, one can diagnose bilateral scotoma as tobacco-alcohol amblyopia by their "racquet" shape. The course of the condition is extremely variable—one patient improved from 20/70 to 20/20 in three days, and one patient did not improve for six months, in spite of the fact that she stopped all tobacco and alcohol for that time, but in a year and a half was almost completely cured. In early cases there are usually no fundus changes; discs may appear hyperemic. Research showed that alcohol *per se* had no chronic effect on the central nervous system, but that alcoholic patients usually had a deficiency of diet. Eight patients who were admitted to hospital care and were given their usual intake of alcohol and tobacco

along with a proper diet experienced as good a rate of recovery as those who abstained from alcohol and tobacco. These patients were given brewers' yeast and cod-liver oil. Research has shown that every alcoholic patient with polyneuritis had a deficient diet, but those with an adequate diet did not have polyneuritis. In routine office practice, however, patients should be told to stop alcohol and tobacco. Dr. Carroll suggested that alcohol amblyopia may be a deficiency disease, but research has not yet shown to what tobacco amblyopia is due.

Discussion. Dr. Carroll in answer to Dr. D. B. Sulouff said that he gives two tablespoons of powdered brewers' yeast in milk four or five times a day; and that Vegex (a teaspoonful in hot water) has been used at Bellevue Hospital with good results. Crystalline vitamin B has also been used successfully, when given intravenously daily. He has also given these patients one ounce of cod-liver oil daily. In answer to Dr. Oast, Dr. Carroll said that he tried giving nitroscleran, and then gave saline, and got as good a result, and that this did not affect the rate of recovery. In answer to a question about foci of infection, Dr. Carroll said that where bad teeth, sinuses, or other such conditions were present, they were not treated until the toxic amblyopia had been cured.

Dr. Clyde E. McDannald said that this report was especially interesting from the standpoint of research, and that he was interested in hearing what the causative factors were in this disease. He said that he was impressed by the infrequency of this condition.

Brittain F. Payne,
Secretary.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

December 16, 1937

DR. WALTER V. MOORE, *president*

EXTENSIVE SCLEROSIS OF CHOROIDAL VESSELS

DR. LEO JACOBS presented the case of a Portugese seaman, unmarried, 43 years of age, who was observed at the Brooklyn Eye and Ear Hospital. He complained of having had poor vision in each eye for the past 12 years. The loss of vision began after he had taken six bottles of Zendejas, a Mexican blood tonic commonly known among sailors, which, when examined was found to be nondeleterious to the eyes.

He had had syphilis at the age of 31 years, which had been treated for six months, and he was then discharged as cured. The general examination was negative. Blood pressure was 132/80; the urine was Wassermann tests were negative.

Ocular examination: Vision 20/200 O.U., could not be improved. Both optic discs showed signs of low-grade atrophy. The retinal vessels were slightly narrow. There was a marked atrophy of the entire retina except in the periphery, where a small amount still remained. The maculae were not distinguishable. The main pathology was located in the choroidal circulation, where the vessels represented various stages of sclerosis from slight perivasculitis narrowing to complete obliteration and replacement by white cords. Some of the blood columns were segmented. These changes presented a great contrast to the overlying retinal vessels which showed only a minimal sclerotic change. The fields were normal in extent for form and color, but many isolated scotomata were present in the central field.

Choroidal sclerosis has the following conditions as possible etiological factors: syphilis—either congenital or acquired; arteriosclerosis, nephritis, tuberculosis, and diabetes. It can be noted that a general condition is always the underlying cause. Choroidal sclerosis is not indicative of a similar process in other parts of the body, as is the case when such a condition is seen in the retinal vessels.

Medical observations in Norway

Dr. Herman Sturcke described the compulsory-health-insurance system showing the position of the medical profession, especially the ophthalmologist, with relation to his patient and the government. There is a marked lack of voluntary hospitals, hence hospital treatment is provided on a large scale by the city, county, and state. Private choice of physicians by the patient is allowed except in the case of indigent patients, who are taken care of by district doctors paid by the government. There is a strong inherent organization of the medical profession with the government, allowing the profession to work out its own problems.

Annotozioni pratiche sulle malattie degli occhi, by G. Quadri, M.D., 1817

Dr. Joseph M. L. Bruno discussed ophthalmological practices and operations as used by Professor G. Quadri. The speaker pointed out that, notwithstanding the many physical difficulties encountered in operating at the time, due largely to the absence of anesthesia and ignorance of bacteriology, ophthalmological surgery was relatively well advanced in those days. Trichiasis and entropion, optical iridectomies, and cataracts were some of the operations mentioned. He pointed out that convex knives were used and discarded in cataract incisions, that paracentesis of the anterior chamber was a common practice as a therapeutic measure, and that white wine was used very much in the same way as boric-acid solution is used today in the irrigation of the conjunctival sac.

Birth injuries of cornea and allied conditions with special emphasis on glass membrane in the anterior chamber

Dr. Allan Hull presented the following case reports: Case 1, of especial interest, was shown with glass membrane of several strands running in a vertical direction, attached to the cornea near the limbus and free in the anterior chamber, giving an appearance of banjo strings. Case 2 was one of a young man with clouding of the deep layers of the cornea with glass-membrane strands extending across the anterior chamber, some attached throughout the entire length of the cornea, and some attached only on the ends, remaining free in the anterior chamber.

Since the advent of the prophylactic forceps, there has been a marked increase in the number of instrumental deliveries, making approximately 10,000 children born annually by forceps in the Borough of Brooklyn. For this reason it is well to bear in mind the etiological factor in glass membrane, clouding of cornea, and other ocular pathology of obscure etiology.

Mortimer A. Lasky,
Secretary-Treasurer.

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HERIDITARY OCULAR DISORDERS OF SENESCENCE

Many of us are prone to think of heredity as a more or less fascinating scientific topic having little or no relation to therapeutics. Hereditary cataract, hereditary coloboma, hereditary refractive errors, hereditary tendency to glaucoma may or may not be susceptible to remedial measures, but we do not ordinarily regard the question whether such conditions are or are not hereditary as being of importance in arriving at a decision as to what degree of success may be expected from therapeutic procedures.

More deliberate consideration suggests that such a decision may be both possible and important for the welfare of the patient. If baldness or premature graying of the hair is due to infection, there may be hope of removing the cause and so avoiding further progress of the disorder or even promoting recovery therefrom. But if the baldness or the grayness was predetermined before the patient was born, in other words is a hereditary characteristic, then little or nothing can be anticipated from any form of treatment.

The same principle is illustrated in the different points of view as to the possibility of finding a remedy for pigmentary degeneration of the retina. If the first appearance and the later progress, or even the ages at which onset and the final condition of more or less complete blindness occur were determined by the germ plasm of the beginning embryo, why hope anything from the feeding of vitamins, from sympathectomy, or from any other remedial effort? Or, if lens changes

of the type generally classified as senile are merely imitative of changes which occurred in the eyes of the patient's forebears for many generations, and were foreordained according to the mysterious principles of heredity from the time of conception, how can we possibly accept the claims made for arrest or cure of such cataractous changes by means of miscellaneous medicaments?

So variable and complicated are the tendencies of heredity, especially as camouflaged by the insistent hammering of early and often poorly recognized environmental influences, that there is often good ground for differences of opinion as to the relative parts played by ancestry and upbringing. The nervous system of the tiny infant begins right soon to receive its environmental molding, through the calm or excitement, the good cheer or complaining, the kindliness or bitter speeches, the order or disorder of those who give it company from day to day. Yet heredity may be falsely credited or blamed for such molding, whereas a different environment from birth might have produced far different results.

Several years ago, upon the basis of a study which included 19 single-ovum and 5 two-ovum pairs of twins between the ages of 55 and 81 years, Alfred Vogt presented the argument that individual senile characteristics occur with so much greater similarity, almost amounting to identity of form, in single-ovum twins as to destroy the hitherto widely accepted beliefs in the production of senile degenerations through factors of environment, or in consequence of the wear and tear of life.

Vogt went on to declare that his study of senile single-ovum twins proved that the stigmata or characteristics of senility had their foundation in the germ plasm (since single-ovum twinning presupposes identity of the germ plasm in both twins) and that senile characteristics manifested themselves necessarily at definite ages and in predetermined form.

In the regions of the face and hairy scalp the study by Vogt just referred to showed that such external characteristics of senility as wrinkles, or loss or graying of hair, were identical in pattern in both single-ovum twins.

Perhaps of even greater importance, as regards the influence of heredity, was the absence of such common changes in certain pairs of twins. Grayness of the hair of the head and also of the hair of the face corresponded in time and pattern, while the development of an exuberant growth of hair on the faces of elderly females showed identity as to thickness, color, and form. If one twin escaped senility in any organ, so, unfailingly, did the other. Complete absence of opacities of the crystalline lens may be just as positively hereditary in two single-ovum twins as complete cataracts in another pair.

In a new paper of deep scientific significance (Klinische Monatsblätter für Augenheilkunde, 1938, volume 100, page 497) Vogt analyzes a larger series of senile and presenile pairs of single-ovum twins, and offers conclusive evidence as to the hereditary character of many pathological conditions whose etiology had hitherto been more or less inaccurately conceived. The conditions dealt with include pinguecula and pterygium; arcus senilis; and changes in the posterior surface of the cornea as well as in the iris, the lens, the vitreous, and the region of the optic disc. The author proposes to discuss refraction in another article.

It is of incidental interest to quote the author's statement that the color of the iris is accepted as an important mark of distinction between single-ovum and two-ovum twins.

Vogt's present 48-page essay is accompanied by 123 illustrations, including por-

traits, colored drawings of the various changes (mostly as seen with the slit-lamp), and fundus photographs.

Other conditions whose at least occasionally hereditary character is claimed by virtue of their behavior in single-ovum twins include circumpapillary and parapapillary atrophy of the choroid, often explained as due to mechanical causes (muscle pressure, accommodation, traction of the optic nerve, and gravity).

As might be anticipated from previous writings (see American Journal of Ophthalmology, 1935, volume 18, page 471), the most important of the author's records relate to senile cataract. The hereditary character of senile cataract, according to Vogt, parallels that of congenital cataract, except that the former is progressive, the latter stationary. Each type of senile cataract is independently inherited. Thus coronary cataract is repeated as coronary, radial cataract as radial cataract, cuneiform as cuneiform, lamellar clefts as lamellar clefts, nuclear cataract as nuclear cataract, and likewise as regards complete lens sclerosis with subcapsular cataract. It is true, however, that the progressive character of senile cataract varies greatly for the individual varieties; the development of the coronary-radial variety being so extremely slow that it is difficult for an individual observer to follow its course, while certain forms of complete sclerosis with secondary posterior subcapsular cataract may be mature for operation within a few months.

Certain authors are skeptical as to the purely hereditary nature of senile cataract. Vogt is disposed to attribute some of these opinions to wishful thinking, since acceptance of the hereditary principle would negative the possibility of non-surgical preventive or remedial treatment.

In Vogt's opinion the idea of a medicine effective against senile cataract is altogether untenable. It would be necessary to assume as many specific toxins as there are hereditary forms of cataract, and correspondingly many specific remedial substances, one for each single form of cataract.

Hereditary characteristics are developed inexorably from the corresponding germ plasm. Would anyone seriously think of correcting a hereditary degeneration of the macula, a hereditary shape of the nose, or any other normal or pathological hereditary characteristic of the body by medicinal or physiochemical means?

Will it be possible to combat cataract by studying the chemistry of cataract? The prospect of success in this field is about equal to that of finding a chemical means of avoiding inherited grayness of the hair, senile or presenile. Where heredity is involved, such efforts are utopian.

Simple reflection, says Vogt, shows that chemical analysis of a hereditary characteristic can never tell anything as to its cause, or therefore anything about its prevention. Chemical analysis of the nerve in a case of Leber's optic atrophy would have certain definite results, differing from those yielded by the normal optic nerve. But could these results, however precise, offer any sort of information as to the possibility of avoiding such an inherited disturbance?

Histological researches and the study of senile single-ovum twins furnish no tangible information as to the part which, according to a few writers, is played by environmental causes in the production of senile cataract. Vogt's findings on this score were negative even when both twins had passed their lives in different conditions of existence and in different regions.

Vogt's final conclusion is that the utopian problem placed before the chem-

ical investigator of senile cataract is that of preventing hereditary characteristics!

W. H. Crisp.

HEPARIN FOR RETINAL THROMBOSIS

Twenty years ago heparin, a substance found within the liver and other parts of the body, was proved to prevent the coagulation of blood. It has been employed as an anticoagulant for blood used for transfusion. Recently it has been obtained in pure form which may be safely injected into the blood in the veins. It has been used with advantage in cerebral thrombosis, and in the last year in the treatment of retinal thrombosis. A case in which this treatment was used has been reported in the Lancet (March 19, 1938) by Holmin and Ploman, of Stockholm, Sweden.

A hospital nurse, of 52 years, noticed sudden dimness of vision in her right eye. The retinal veins were dilated and there were hemorrhages along them. On the third day, vision being 0.2, intravenous injections of 5-percent heparin were made, every four hours while the patient was awake. This was continued three or four times a day for 10 days, when vision had risen to 0.8. At the end of three months the eye had vision of 1.; that is, standard vision. The remedy removed the obstruction from the vein, and also hastened the absorption of the retinal hemorrhages.

The prognosis for retinal thrombosis is generally better than that for retinal embolism. It usually ends in partial restoration of vision, whereas retinal embolism often leads to complete, permanent blindness. However, the course of this case seems to indicate that the use of heparin tends to hasten the cure and make it more complete. In this case the obstruction seemed to be in the central retinal vein. Frequently, with the ophthalmoscope, the particular branch of the retinal vein that has been occluded can be identified, and the effect of the heparin on the clot may be watched from day to day.

Since heparin in the blood stream favors the breaking up and removal of the clot, it might be found of considerable value in retinal embolism. It certainly should be tried as quickly as possible after the loss of sight has been noticed. Retinal thrombosis is often confused with embolism; however, in either case, heparin is indicated. So far as is known it is a remedy free from serious danger. In the eye we would be justified in pushing it, and watching its effects. Heparin would certainly be a safer substance with which to experiment than some of the other anticoagulants; for instance, the aso-dyes, such as "Chicago blue 6B," suggested by Rous, or "chlorazol pink."

Edward Jackson.

BOOK NOTICES

FUNDUS OCULI DIAGNOSTICA OFTALMOSCOPICA. By Prof. Q. Di Marzio. Clothbound, 212 pages, 212 figures in color. Rome, Stab. L. Salomone, 1937. Price not stated.

This is as beautiful an atlas of the fundus oculi as has ever been published. In extensiveness and completeness it far exceeds any other atlas of the eye-grounds. There are 212 colored illustrations most of which measure five inches square.

The subjects are well chosen, colors very true to life. The text describes the pictures fully and accurately, in almost all cases giving the clinical history of the patient from whom the illustration was taken. In many of the optic-nerve lesions visual fields, X rays, and photographs of the patient are included.

It is unfortunate for the American ophthalmologist that the text is written in Italian. However, it is so simple that a reasonable familiarity with Latin and French permits one to understand it without recourse to the dictionary. The book would be a valuable addition to any ophthalmic library.

Lawrence T. Post.

INTRODUCTION TO OPHTHALMOLOGY. By Peter C. Kronfeld, M.D. Clothbound, 331 pages, 32 figures, 5 plates, index and ophthalmic dictionary combined. Charles C. Thomas, Publisher, Springfield, Illinois, 1938. Price $3.50.

On first picking up the book, the reader is impressed by the good appearance, excellent binding, clear printing, and readable page. Obviously much thought and care have been given to these extrinsic factors.

The author states his intention has been "To formulate the principles underlying that portion of ophthalmology which is a necessary part of basic medical education." If this has been accomplished the book has a very real value for teaching in medical schools because this is all that should be attempted in ophthalmic teaching of the undergraduate. Again to quote from the author's preface: "The material presented pertains principally to the pathogenesis of disease. The details of diagnosis, of methods of examination, and of treatment have been omitted." This seems a very logical method, and the author has carried out this data faithfully. The book is interestingly written and many important points that are often overlooked are stressed.

The first chapter is of necessity devoted to anatomy, and succeeding chapters to diseases of the various elements in the eyeball. A consideration of injuries, vascular disease, and the intraocular pressure is then taken up. Neoplasms, the optic nerve, visual pathway, the pupil, and motor anomalies are presented, and finally a few pages are used for consideration of some of the elements of refraction. Plates are in black and white. They illustrate very well a dozen common intraocular conditions.

This book should prove of real value to the teacher of undergraduates. A course modeled on it would include the essentials and give an excellent theoretical outline. Any medical student who had a good knowledge of its contents would be conversant with the ophthalmic facts necessary to him as a general practitioner. Lawrence T. Post.

ALLERGISCHE AUGENERKRANKUNGEN (Allergic diseases of the eye). By Arnold Löwenstein. 72 pages. Basel & Leipsig, S. Karger, 1938.

This monograph comprises a review of diseases of the eye associated with or due to an allergic state. It therefore represents a summary of the literature together with the observations and comments of the author, thus affording a brief but competent presentation of the subject. That the number of allergic diseases of the eye discussed does not represent the total is the author's opinion, and accordingly the future will reveal even more manifestations. Löwenstein advises caution in explaining inflammations of uncertain pathogenesis as allergic, a fault it must be admitted becoming more and more common. The difficulties of diagnosis are acknowledged as faulty history, preconceived notions of the patient, unreliability of cutaneous reactions due both to the technical difficulties in eliciting reactions and to the interpretation of these tests. Thus, as contrasting examples, hay fever and vernal catarrh are the

most frequent allergic conjunctivitides encountered, the former responding favorably to skin test and treatment, the latter responding to neither.

Among other things the author makes particular issue of the following manifestations of ophthalmic allergy. Phlyctenular conjunctivitis is considered as accompanying hypersensitiveness of different origins, although most commonly seen in tuberculin allergy. Parenchymatous keratitis is regarded as an example of anaphylactic response stimulated by antigens arising not from the spirochaete but from degradation products of the corneal tissue. On the other hand, there is also a variety of hypersensitive parenchymatous keratitis unrelated to syphilis. This is characterized by a dusky-red injection of the eyeball, severe pain, diminished tonicity, progressive parenchymatous inflammation of the cornea eventually leading to marked opacity. This condition may be seen experimentally, and clinically in trachoma, corneal trauma, and after various surgical procedures.

Trachomatous pannus is believed to be an allergic manifestation in that the inflammatory and scarring processes invading the subconjunctival connective tissue cause a nutritional disturbance of the cornea; this in turn initiates tissue destruction and adsorption of antigen which finally creates the allergic state. While this may be a plausible hypothetical explanation, there is reason to believe that the cornea is actually invaded by the virus of trachoma and it is the reviewer's opinion that this fact alone is sufficient to create conditions for the formation of pannus. Tuberculous iridocyclitis is likewise regarded as an allergic manifestation, while the author feels no conclusive proof has been advanced to classify sympathetic ophthalmia and phacoanaphylactic endophthalmitis as hypersensitive reactions. Chalazion is considered as allergic and arising from the degenerated epithelium of the meibomian gland, the resultant histological picture being that of an allergic nodule. The allergic nodule observed frequently in the papillary form of hypersensitive reaction consists of lymphocytes, epithelioid and giant cells, with central regressive metamorphosis, similar in fact to the nodules originally described by Aschoff in rheumatic myocarditis and considered by Klinge as an allergic alteration.

L. A. Julianelle.

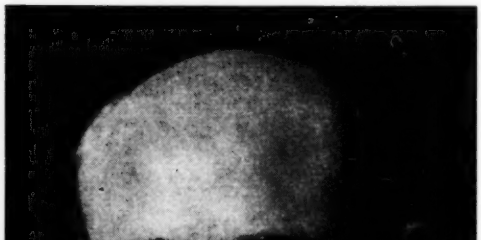
OBITUARY

JOHN MARTIN WHEELER
1879-1938

John Martin Wheeler was born on November 10, 1879, in Burlington, Vermont. His parents were Henry Orson Wheeler and Elizabeth Lavinia (Martin) Wheeler. The Wheeler family had come to America in the early days from Cranefield, Bedfordshire, England, and settled at Concord, Massachusetts. John Wheeler's father, a lawyer, served as superintendent of schools in Burlington, Vermont, for 33 years.

John Wheeler received his early education in the public schools of Burlington. On completion of this he attended the University of Vermont, from which he received the degree of A.B. in 1902. Three years later he was graduated in medicine from the same institution and in 1906 received the M.Sc. degree. During the years 1906 and 1907 he was instructor in anatomy. The next year and a half was spent in the New York Eye and Ear Infirmary as an intern. From that time New York became his home. Natural ability, hard work, and a charming personality combined to bring about his continuous progress to the highest rank in ophthalmology. He was an im-

portant figure in all of the national ophthalmological societies, having served on the councils of the American Ophthalmological Society and the American Academy of Ophthalmology and Otolaryngology. He was elected president of



John Martin Wheeler

the latter organization in 1933. Manifold demands were made on him because the benefit of his technical knowledge, good judgment, and wisdom was so much needed.

Dr. Wheeler was appointed professor of ophthalmology at Columbia University in 1928 and three years later, when the Eye Institute was built at the Columbia-Presbyterian Medical Center, he was invited to become its director. Under his leadership this rapidly became one of the most outstanding ophthalmic centers in America.

His special interest was surgery, and in this he had no peer. His patients came from all parts of the world, and he was constantly busy in his operating room. This theater was constructed after his own idea. It was designed with a circular visitors' balcony overhanging the operating table, with glass windows through which observers with the aid of opera glasses could get a very satisfactory view.

To watch Dr. Wheeler operate was a great privilege. Fortunately, many were able to enjoy it, and by actual demonstration he directly aided ophthalmic surgery in this country. As must be so of all great surgeons, the outstanding feature of his success was his invariable good judgment. Of less importance, but a vital factor also, was his beautiful technique. He truly had magic in his fingers. Originality was a prominent feature of his surgery. This was evidenced especially in his plastic cases, plastic surgery being a branch in which he was particularly interested and to which he made notable contributions.

It was his way to ask opinions of whomever he was with. He was a good listener. Quite free from the habit of interrupting, he would, in fact, often wait a noticeable time after the speaker had finished before replying. His own suggestions were usually made with a twinkle in his eyes—a very characteristic feature which was never far away and which was one of his most lovable attributes, for he was endowed with a delightful sense of humor.

It was a disappointment that Dr. Wheeler did not write a book on plastic surgery of the eye. Had he had the time it would have been a contribution that he would have enjoyed making, for he felt strongly that ophthalmologists did not do nearly so much in this field as they should, and that all plastic work about the eyes should be performed by eye surgeons.

Another of his major interests was the training of young men in the specialty. He quickly gathered around him a strong organization, complete in every department, and internships and residencies in the Presbyterian Eye Infirmary were greatly sought after. He believed in long institutional training. The service that he offered was originally for three years and had recently been increased to four.

Though well known to ophthalmologists for many years, he first received popular notice through his selection by the King of Siam to operate on his eyes. Dr. Wheeler was naturally a modest and retiring man, so that the publicity in connection with this operation was distasteful to him. It did, however, serve a purpose in that it directed a great deal of surgery to him and permitted him to accumulate a vast experience. So expert was he that when, three years before his death, the use of one eye was lost to him because of a malignant growth, he was able after a brief period of practice to continue operating apparently as efficiently as before he was deprived of binocular vision. His reaction to this trouble was typical of his life's philosophy of quietly carrying on. The period of readjustment was extraordinarily brief, and thereafter no one would have realized that he had passed through a terrifying ordeal. Through these days, as now for many years, there walked beside him a devoted and courageous figure, she who had borne his four children and made his home a charming and happy rendezvous for their many mutual friends; a wonderful background for the cultivation of equanimity.

In 1928 Dr. Wheeler received an honorary degree of D.Sc. from the University of Vermont, and in 1933 from Middlebury College. In 1931 he was awarded the decoration of Commander of the Order of the Cross of Siam. In the same year he received the Leslie Dana medal for distinguished service in the conservation of sight. But to list his honors and his society connections is unnecessary for readers of this Journal because these are well known to them.

His was the very heart of ophthalmology. He was known and loved by all. He was the ideal of the younger men—in whom he was vitally interested.

Dr. Wheeler had seemed so well and so happy at the meetings in San Francisco last June that he gave promise of many years of usefulness. He had experienced a slight heart attack one year before his last illness, but did not consider this very seriously and did not curtail his enormous activity. A week before his death, while working at his summer home, he had a second attack, from which he was apparently improving when without warning death came.

It is tragedy that he was taken while life's tide was at the flood. We shall miss him terribly though we cannot feel that he has truly gone. He colored brightly so many lives. In them his spirit lives.

Lawrence T. Post.

CORRESPONDENCE

VITAMIN THERAPY

June 17, 1938

In an abstract in the June issue of the American Journal of Ophthalmology, reference is made to an article of mine in the Archives of Ophthalmology. A diet rich in vitamin B, not vitamin D, was used in this work and, of course, yeast is rich in vitamin B.

Probably this was a printer's error, but I should appreciate a correction if it is not too inconvenient.

(Signed) Frank D. Carroll, M.D.

ABSTRACT DEPARTMENT

EDITED BY DR. WILLIAM H. CRISP

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is only mentioned in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

1

GENERAL METHODS OF DIAGNOSIS

Berens, Conrad. **Stereoscopic cards in color for children: series A.** Amer. Jour. Ophth., 1938, v. 21, July, p. 785; also Trans. Amer. Ophth. Soc., 1937, v. 35, p. 350.

Dashevsky, A. I. **Clinical angioscotometry; a new method, with the use of different contrast test objects.** Arch. of Ophth., 1938, v. 19, March, pp. 334-353.

The method described permits exact measurements of angioscotomas and the detection of changes in the scotomas not heretofore possible. It is based on the principle of campimetric examination with contrast test objects. The experiments reported confirm the findings of others that angioscotomas are the shadows of the retinal vessels and the lymphatic perivascular spaces. The variations found in persons with normal eyes but suffering from high intracranial tension and changes in circulation are discussed. This method permits the detection of the earliest stages of a lymphatic disorder in the posterior segment of the eyeball and, when combined with the pilocarpine test, offers a greater possibility of obtaining positive results in the prodromal stage of glaucoma. It also permits the study of the influence of various drugs on the circulation of the blood and lymph of the eye. J. Hewitt Judd.

Feldman, J. B. **Practice of dark adaptation.** Arch. of Ophth., 1938, v. 19, June, pp. 882-901.

The subject of dark adaptation is reviewed as to theory, technique, and clinical applications. The author's instrument for quantitative determination is described. Graphs of characteristic conditions are included.

T. E. Sanders.

Ferree, C. E., and Rand, G. **A glareless bed reading and examining lamp with variable intensity and placement of light.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 882-890.

Foster, J. **Binocular fixation for scotometry at one meter.** Brit. Jour. Ophth., 1938, v. 22, July, pp. 426-429.

Two models are described: the one using a chin rest and being more suitable where illumination of the scotoma screen is variable, and the second without a chin rest and with the illumination of the Bjerrum screen a constant quantity. (Illustrations.)

D. F. Harbridge.

Foster, J. **Notes on optical instruments and devices.** Brit. Jour. Ophth., 1938, v. 22, July, pp. 430-433. (See Section 2, Therapeutics and operations.)

Good, Palmer. **A standardized apparatus for testing the visual acuity of the preschool child.** Arch. of Ophth., 1938, v. 19, Feb., pp. 251-252.

The apparatus has the appearance of a flashlight over which are fitted transparent, washable celluloid discs. There are seven discs on which the Snellen E varies in size from 20/15 to 20/100 and which, when transilluminated, have an illumination of ten foot-candles.

J. Hewitt Judd.

Lijo Pavia, J. **Eyeground stereoscopic chromoretinography.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1936, v. 1, pp. 171-173.

The author emphasizes the advantage of using color photography to completely differentiate pathologic conditions of the eyeground. Black and white photography will not differentiate pigmentary changes from hemorrhages in the eyeground. Lijo Pavia has been able to obtain stereoscopic color-photographs of the eyeground, nine of which are used to illustrate the present article.

Ramon Castroviejo.

Lobeck, Erich. **A new use for the achromatic double lens (f = 7 and 10 cm.) in the slitlamp examination.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 658-660.

During the last six years, the author has used the front double-lens on the original model of the Gullstrand slitlamp (before Comberg's modification) for examining both eyes without a complete change in position of the slitlamp arm. With the arm in position for studying say the left eye with the lens of 7-cm. focus, then to examine the right eye, the lens with a 10-cm. focus is revolved into position and the slitlamp arm swung a little. H. D. Lamb.

McLean, J. M., and Goebel, A. **A new model gonioscope.** Arch. of Ophth., 1938, v. 19, June, pp. 983-985.

A portable gonioscope stand is described for use with the corneal microscope and the hammer lamp.

T. E. Sanders.

Woods, A. C., Burky, E. L., and Friedenwald, J. S. **Experimental studies of ocular tuberculosis. 1. Relation of ocular sensitivity to cutaneous sensitivity in the systemically infected rabbit.** Arch. of Ophth., 1938, v. 19, Feb., pp. 229-235.

The results of an investigation on the relation of cutaneous and ocular sensitivity in the normal rabbit infected by systemic injection of human tubercle bacilli are reported. Ocular sensitivity was found to develop synchronously with cutaneous sensitivity, the nondiseased eyes participating in the general development of tissue sensitivity. With minor variations, during the course of this self-limited disease in the rabbit, cutaneous and ocular sensitivity ran fairly parallel, reaching their peak from six to eight weeks after systemic inoculation, declining slightly as the animal overcame the infection, but being definitely present for at least nine months after infection, when the last rabbits were tested. J. Hewitt Judd.

Woods, A. C., Burky, E. L., and Friedenwald, J. S. **Experimental studies of ocular tuberculosis. 2. Relation of ocular activity to ocular sensitivity in the normal rabbit infected by injection of tubercle bacilli into the anterior chamber.** Arch. of Ophth., 1938, v. 19, Feb., pp. 236-245.

When the normal rabbit was inoculated with tubercle bacilli in the anterior chamber and the primary tuberculous focus lay in the eye, ocular sensitivity began to develop about the second week after inoculation and reached its height in about four weeks. The eyes showed a slowly progressive tuberculous inflammation during the first few weeks, which became acute, with caseation and necrosis, as the ocular sensitivity developed to maximum. Active tuberculous inflammation and ocular sensitivity persisted steadily up to the sixteenth week, although about the eighth week there was some loss of vascular bed by necrosis. From the sixteenth to the twenty-first week, when the experiment was terminated, the ocular sensitivity faded and the active inflammation subsided synchronously, the eyes thereafter showing evidence of scarring and repair. In the final stage of comparative inactivity there were occasional minor exacerbations of inflammation. There was suggestive evidence that these exacerbations of activity were related to the presence or return of the ocular sensitivity.

J. Hewitt Judd.

Woods, A. C., Burky, E. L., and Friedenwald, J. S. **Experimental studies of ocular tuberculosis. 3. Relation of cutaneous sensitivity to ocular sensitivity in the normal rabbit infected by injection of tubercle bacilli into the anterior chamber.** Arch. of Ophth., 1938, v. 19, Feb., pp. 245-250.

A local tuberculous focus in the eye of an otherwise normal rabbit produces only a low grade of cutaneous sensitivity. This cutaneous sensitivity appears the second week after inoculation and is distinctly less than is observed after systemic inoculation. The second eye acquires a definite sensitivity to purified protein derivative after inoculation of the fellow eye. This appears to be more constant, and possibly of higher degree, than the cutaneous sensitivity. There is no relation between the cutaneous sensitivity and the sensitivity of the diseased eye in such a rabbit. Cutaneous sensitivity gives no idea of the degree of ocular sensitivity present.

J. Hewitt Judd.

2

THERAPEUTICS AND OPERATIONS

Brown, A. L. **Use of typhoid-H antigen before intraocular operations.** Arch. of Ophth., 1938, v. 19, Feb., pp. 181-183.

As a prophylaxis in cases in which postoperative inflammation is feared, typhoid-H antigen is given intravenously from 48 to 72 hours before operation. The antibody titer of the aqueous is raised automatically by the ocular incision. The new aqueous is rich in H antibodies derived from those formed in the blood by the previous injection. In one hundred cases in which this method was used, postoperative inflammation occurred only in one. The author also suggests that the antigen be given immediately in cases of perforation of the globe. J. Hewitt Judd.

Cornet, Emmanuel. **Semi-retrobulbar injection in intraocular operations.** Ann. d'Ocul., 1938, v. 175, April, pp. 324-325.

Injection behind and above the globe, through the upper lid, provides paralysis of the superior rectus and hypotony,

both advantageous in cataract and glaucoma operations. John M. McLean.

Cutler, M., Jaffe, H. L., and Grossman, A. **Irradiation of the eye and protective devices.** Amer. Jour. Ophth., 1938, v. 21, July, pp. 747-754.

Davids, Hermann. **The treatment of ocular tuberculosis.** Zeit. f. Augenh., 1938, v. 94, April, p. 305.

The author discusses the therapy of ocular tuberculosis in general terms without recording specific data. His conclusions are of value because he has been actively interested in the subject ever since he worked with tuberculin under the guidance of A. Hippel. He believes that tuberculin is of inestimable value but that it must be used with great attention to many details in the individual patient. High altitude, non-specific protein therapy, and radiotherapy are also of value and can be used in conjunction with tuberculin.
F. Herbert Haessler.

Foster, J. **Notes on optical instruments and devices.** Brit. Jour. Ophth., 1938, v. 22, July, pp. 430-433.

Described and illustrated are the following: an ophthalmic needle holder, a disc to bring out the glaucoma halo, a level for the trial frame, an instrument holding a concave and a convex lens and also a cross cylinder, and a retinoscopy rack. D. F. Harbridge.

Gifford, S. R. **Physical therapy in ophthalmologic practice.** Arch. of Ophth., 1938, v. 19, Feb., pp. 171-180; also Trans. Amer. Acad. Ophth. and Otolaryng., 1937, 42nd mtg., p. 94.

Phototherapy is apparently indicated only in herpetic and a few other forms of superficial keratitis. Roentgen therapy in small doses may replace it, since some cases of keratitis were benefited after phototherapy had failed. The infrared lamp is superior to heating pads and moist hot packs. Local short-wave diathermy is the most efficient method for producing heat in the deeper tissues and is indicated in cases of cellulitis of the lids and orbit, and those of acute dacryocystitis and chronic uveitis. General fever therapy is valuable in gonorrheal ophthalmia, interstitial keratitis and luetic optic atrophy. Roentgen therapy is indicated in cases of obstinate blepharitis and certain forms of keratitis. J. Hewitt Judd.

Hambresin, L. **Pyretotherapy in ophthalmology.** Arch. of Ophth., 1938, v. 19, April, pp. 497-514.

Pyretotherapy or treatment by fever produces modifications in the organism which either make other therapeutic agents more active or the organism more receptive to those agents. The author discusses the principal methods of fever therapy, malariotherapy, dmelcos, pyrifer, sulphur in oil, the Kettering hypertherm, and short waves, and indicates the advantages of each. The chief indications are simple syphilitic optic atrophy, syphilitic pupillary disturbances, syphilitic arachnoiditis of the optic chiasm, keratitis, and uveitis. Pyretotherapy gives best results when instituted early. J. Hewitt Judd.

Kapuscinski, W. J., Jr. **The action on the eyes of rats of a locally administered vitamin A and the effect upon this action of vitamin D.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 667-672.

Preparations of vitamin A were instilled or, in the form of an ointment, rubbed into the conjunctival sac of rats twice a day for about two months. The ointment produced much less effect than the drops. The first group in-

cluded seven white rats which were kept in the dark. In one to two weeks after the start of the experiment, all the animals presented loss of hair in the form of a ring around the eyes and mouth, inflammation of the conjunctiva, and narrowing of the palpebral fissure. In three other white rats which were always kept in daylight, the same changes occurred as in the first group, although less intensively. When grayish-colored rats were treated in a like manner, the same changes were very mild. Lastly, four small white rats kept in the dark first received for two weeks instillations in the eye of vitamin D. Later vitamin A was administered, with the appearance of very mild or no changes. Both daylight and vitamin D were thus found to inhibit the action of vitamin A. H. D. Lamb.

Kirby, D. B., and Macnie, J. P. **The use of cadaver and animal eyes for training and experience in surgery.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 904-906.

Koller, Carl. **Local bloodletting in ophthalmic practice.** Arch. of Ophth., 1938, v. 19, March, pp. 331-333.

Local bloodletting has fallen into disuse in recent years but still is very beneficial for a number of ocular conditions, especially when congestion is a prominent symptom. The author describes his mode of procedure and advocates it in persistent episcleritis, iritis, and iridocyclitis, chronic trachoma with exacerbations, subacute conjunctivitis, and relapsing abrasion of the cornea.

J. Hewitt Judd.

Laval, Joseph. **Avertin anesthesia for ophthalmic operations.** Arch. of Ophth., 1938, v. 19, May, pp. 714-718.

The use of avertin as a basal anesthetic in ophthalmic surgery is discussed, including technique of administration, indications, and contraindications. The advantages are described and five cases are reported.

T. E. Sanders.

McGavic, J. S., **Fever therapy for ocular diseases.** Arch. of Ophth., 1938, v. 19, May, pp. 769-796.

The subject of induced hyperpyrexia in ocular disease is reviewed, including a description of the technique and the results in fifty cases of diseases of the eye. The procedure was most efficacious in the treatment of gonorrheal conjunctivitis, syphilitic interstitial keratitis, and syphilitic iridocyclitis. It is suggested that it might be of value in other ocular inflammations. T. E. Sanders.

Rambo, V. C. **The effects of sulfanilamide as determined in the eyes of rabbits.** Amer. Jour. Ophth., 1938, v. 21, July, pp. 739-746.

Rezende, Cassio. **Some homeopathic remedies of real value in ophthalmology.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1936, v. 1, pp. 201-212.

This article can hardly be read without a smile. It is of no value to ophthalmology.

Schwartz, L. H. **Clinical experiments with one-percent solution of epinephrine hydrochloride.** Arch. of Ophth., 1938, v. 19, June, pp. 976-981.

The effects of one-percent epinephrine hydrochloride in various ocular conditions including conjunctivitis, keratitis, iritis, glaucoma, dacryocystitis, and myopia are discussed. Over two hundred cases have been treated without untoward effects and with good results. T. E. Sanders.

Weintraub, J. D. **Strength of epinephrine compounds in ophthalmotherapy.** Arch. of Ophth., 1938, v. 19, May, pp. 759-761.

A new epinephrine ophthalmic ointment using an oxycholesterol base is described. It is suggested that the strength of epinephrine preparations be based on chemical normality so as to avoid confusion in comparing the equivalent strengths of the various preparations. T. E. Sanders.

Yudkin, A. M. **Vitamins in treatment and prevention of ocular diseases.** Arch. of Ophth., 1938, v. 19, March, pp. 366-377.

The observations previously reported in the literature are reviewed and the author's results from vitamin therapy are discussed. Vitamin A apparently is useful in the treatment of corneal inflammations and chorioretinal disturbances and enhances the normal function of the rods and cones. Vitamin-B complex is valuable in the treatment of toxic amblyopia, especially tobacco-alcohol amblyopia. A combination of vitamin-A and vitamin-B complex is helpful in those cases of ocular inflammation thought to be caused by focal infection. Vitamin C is beneficial for extravasation of blood in the vitreous, choroid, and retina but lemon juice seems to clear the extravasation of blood and edema much more rapidly than synthetic vitamin C. Vitamins D and E apparently have no definite therapeutic value. J. Hewitt Judd.

3

PHYSIOLOGIC OPTICS, REFRACTION, AND COLOR VISION

Barri, Clara. **The concept of abnormal retinal correspondence; a theoretical analysis.** Arch. of Ophth., 1938, v. 19, March, pp. 409-424.

In this review the author defines and analyzes the concept of this condition and presents some experimental evidence in support of a new hypothesis that the two retinas do not correspond exactly by either cell-to-cell or retinal-to-cortical area but that the patient's localizing of his images is a perceptual interpretation of his visual experience, his conditioning by past experiences, and his knowledge of the object from touch and audition, as well as from the clues of his ocular convergence-accommodation adjustments.

J. Hewitt Judd.

Beach, S. J., and McAdams, W. R. **Benzedrine in refraction.** Trans. Amer. Ophth. Soc., 1937, v. 35, p. 221.

Atropine and benzedrine sulphate are synergistic in their cycloplegic action and can be administered in combination in the office to children, thus obviating the necessity of two visits. The duration of the cycloplegia is much shortened. A similar action has been noted in combination of homatropine and benzedrine, so that cycloplegia induced by one instillation of the combination is as effective as and of shorter duration than repeated instillations of homatropine alone. David Harrington.

Bogoslovski, A. I. **Changes in critical frequency of luminous flickering to the character of a conditioned reflex.** Arch. d'Opht., 1938, v. 2, March, pp. 219-227.

This highly technical dissertation is hardly adapted for abstracting but is mentioned here for the benefit of those performing special research on the subject. If the experiments, without an auditory exciter, were repeated several days in succession, the acquired reaction became extinguished and the curves of critical frequency of the flickerings reassumed their previous regu-

lar aspect. Such changes were interpreted as sensorial reflexes conditioned by the time which had elapsed since the beginning of adaptation to darkness. W. H. Crisp.

Brown, E. V. L. **Net average yearly changes in refraction of atropinized eyes from birth to beyond middle life.** Arch. of Ophth., 1938, v. 19, May, pp. 719-734; also Trans. 15th Internat. Ophth. Congress, 1937.

The net average yearly changes in refraction from birth to the end of the 51st year have been studied in the atropinized eyes of 1,203 persons. The following changes were noted. Hyperopia increases each year until the end of the seventh year. Myopia increases and hyperopia decreases rapidly from 8 to 13 years. From 14 to 20 years this increase continues each year but at a rate barely half that of the previous period. The increase of myopia after 20 years is practically negligible.

T. E. Sanders.

Clark, L. B. **Dark adaptation in Dineutes.** Jour. Gen. Physiology, 1938, v. 21, Jan. 20, pp. 375-382.

The level of dark adaptation of the whirligig beetle was measured in terms of threshold intensity calling forth a response. The intensity of the adapting light determines the level at which dark adaptation will begin but follows the same course irrespective of the level of light adaptation. T. E. Sanders.

Elsberg, C. A., and Spotnitz, H. **Are vision and the olfactory sense governed by the same laws? A comparison of the results of quantitative functional tests of vision and of the sense of smell and its significance.** Bull. Neurol. Inst. of New York, 1937, v. 6, Dec., pp. 421-429.

The authors show that the formulas for dark adaptation hold for fatigue of smell. They believe that dark adaptation and olfactory fatigue are like processes and that basically both processes are cerebral. T. E. Sanders.

Fink, W. H. **The dominant eye.** Arch. of Ophth., 1938, v. 19, April, pp. 555-582; also Sec. on Ophth., Amer. Med. Assoc., 1937, 88th mtg., p. 221.

This discussion deals with the technique for testing ocular dominancy, the nature of ocular dominancy, the influence of ocular dominancy on the ocular mechanism, and the influence of ocular dominancy in the management of ocular problems. No definite conclusions are drawn, but there is some evidence pointing to the importance of maintaining the dominant eye as the master eye when considering surgery, and of utilizing the test for dominancy as a test for malingering. (Discussion.)

J. Hewitt Judd.

Gillessen, P. **Experimental observations on the question of contractility of the lens fibers.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 598-619.

Experimental observations on the biology of the lens were carried out in rabbits, cats, dogs, and rhesus monkeys. After dilatation of the pupil with atropine, a solution in a fine capillary pipette is introduced into the cortex near the equator of the lens of an anesthetized animal. Solutions of acetylcholin and histamin, being stimulants to the parasympathetic system, produce contraction of the lens-fiber cells when introduced within the lens. This conclusion is inferred from the change in refraction noted by skiascopy before and after the injection. It is found that in about fifteen minutes the hyperopia generally present becomes less and

even changes into myopia. Usually at the end of another fifteen minutes the refraction has returned to the condition before the injection. From this, it is concluded that the lens fibers have relaxed.

H. D. Lamb.

Glaser, J., and Lerner, M.C. **Cyclic vomiting of ocular origin.** Amer. Jour. Dis. of Children, 1937, v. 53, May, p. 1273.

Five cases at ages ranging from two to seven years are reported. Atropine refraction revealed moderate hyperopia with mild or moderate astigmatism and in one case moderate mixed astigmatism. Glasses were prescribed in all the cases. Astonishingly rapid disappearance of symptoms resulted in one case. In the others the relief was remarkable and permanent.

The authors advise atropine refraction regardless of age in cases of cyclic vomiting where there is no other discoverable cause. F. M. Crage.

Graham, C. H., and Kemp, E. H. **Brightness discrimination as a function of the duration of the increment in intensity.** Jour. Gen. Physiology, 1938, v. 21, May 20, p. 625.

A very technical article unsuitable for abstracting. (12 references.)

Irmak, S. **Concerning vision of nomads in Asia Minor.** Deut. med. Woch., 1938, May 6, p. 677.

This work was done at the Institute for General Physiology of the University of Istanbul. The author states that there are still one-half million nomads of Turkish origin in Asia Minor. She examined a great number and sought to measure visual acuities and visual angles. She states that these nomads have the greatest visual acuity of any race examined to date. The minimum visual angle was 5°5″. In more advanced age two to three times "normal" vision was observed. In one case visual acuity of nine times "normal" was seen. She concludes that the best visual acuities appear to be due to heredity of the dominant type. Theodore M. Shapira.

Kyrieleis, Werner. **Observations on the course of dark adaptation by a new method having an automatic marking of the position of the threshold.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 564-597.

Movement of the screw regulating the Aubert diaphragm of the adaptometer is automatically recorded on a kymograph drum. It is possible then to make ten and more determinations of the threshold each minute. Five a minute is best. The author discusses for adaptation to dark the general course of the curves, individual differences and the individual constant of the course, the course in twins, the influence of preliminary illumination of varying duration and intensity, the influence of the width of the pupil, and the action of brief light stimulus (exposure of both eyes, of one eye, and hemianopic).

H. D. Lamb.

Ludvigh, E., and McCarthy, E. F. **Absorption of visible light by the refractive media of the human eye.** Arch. of Ophth., 1938, v. 20, July, pp. 37-51.

The authors review the literature and present a description of the apparatus and the method of procedure in their method of measuring the absorption of visible light by the ocular media. They present the results of the measurements on four human eyes, which have been calculated on the basis of an average age of 21.5 years instead of the actual age which was 62 years. These transmission values are shown in a table and

graphs. The average transmission throughout the visible spectrum is 0.531 percent. The apparent photopic brightness of an equal energy source is only 56.9 percent of the brightness that it would have if the energy were directly incident upon the retina, and the apparent scotopic brightness is 49.8 percent.

J. Hewitt Judd.

Motolese, A., and Berardi, M. **Notes on heredity of ocular diseases.** Boll. d'Ocul., 1937, v. 16, Nov., pp. 1101-1117.

From the data obtained in accurate observations on corneal astigmatism in 42 families, the writer comes to the conclusion that with the exception of irregular astigmatism corneal astigmatism is a hereditary taint and that its transmission is effected from father or mother to the children of both sexes. Astigmatism may be considered a direct hereditary anomaly of refraction.

M. Lombardo.

Nelson, F. **Contact lenses with spheric optic and aspheric haptic part.** Amer. Jour. Ophth., 1938, v. 21, July, pp. 775-779.

Obrig, T. E. **Molded contact lenses.** Arch. of Ophth., 1938, v. 19, May, pp. 735-758.

The technique for fitting the new molded contact lens made from a casting of the anterior portion of the eye is described in detail. The principal difficulty in securing comfort with contact lenses, which is due to pressure at the limbus horizontally, is removed, as these lenses are molded to avoid this pressure as well as to give a good fit in the scleral portion. Measurements of the cornea obtained from the casts are considerably larger than generally believed, averaging 12 by 13.5 mm.

T. E. Sanders.

Ogle, K. N. **Mathematical analysis of the longitudinal horopter.** Pflügers Arch. f. d. ges. Phys., 1938, v. 239, pt. 6, pp. 748-766.

The author presents a mathematical investigation of the longitudinal horopter curve on the basis of experimental findings, but not of the theoretical intervals. It is shown that the relative size of the visual angle of the two eyes, belonging to any given point of the horopter curve, could be expressed in a regular algebraic relationship, starting from the assumption that the longitudinal horopter curve represents a part of a spherical section whose form is determined by a single parameter. It is further shown that an asymmetry, that is an apparent turning of the horopter curve around the fixation point, can be traced to an inequality of the retinal images. The paper concludes with explanation of the application of analytic methods to the empirical horopter curve, with some illustrations, and individual questions of the horopter problem are discussed. W. H. Crisp.

Olsho, S. L. **Vertical prism values in commonly used bifocal lenses.** Arch. of Ophth., 1938, v. 20, July, pp. 95-104.

This review includes a discussion of the prismatic effect for both distance and segment components, and gives a very clear and concise description of the method of determining the prismatic effects in any combination of lenses.

J. Hewitt Judd.

Schneck, Nathan. **An improved trial frame and temples.** Arch. of Ophth., 1938, v. 19, June, p. 981.

A trial frame is described in which the bridge is replaced by a nose grip. The frame can be adjusted so as to fit a child. T. E. Sanders.

Wald, George. **Area and visual threshold.** Jour. Gen. Physiology, 1938, v. 21, Jan. 20, pp. 269-287.

The variation of retinal threshold with field area was measured, and it was found that at 15 degrees above the fovea, an increase in field diameter from 10 to 15 degrees reduced the threshold sevenfold and at 25 degrees tenfold. T. E. Sanders.

Zubler, Rudolf. **The entoptic demonstration of the yellow color in the macula centralis retinae.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 633-646.

For direct entoptic examination of the macular yellow color, the red-free arc light with direct current, as devised by Vogt, is found best of all to make the color distinct. The present writer uses Vogt's method of focusing the red-free rays with a convex lens upon the sclera on the nasal side. The width of the yellow area, 0.78 to 0.75 mm., determined by this entoptic method corresponds well with that obtained with the ophthalmoscope and red-free light. Parallactic relations of the yellow oval observed entoptically in red-free light show that it lies in the inner retinal layers. Thus it is really a yellow material and not a light reflection from the choroid or sclera. When greenish-blue or blue light is focused upon the sclera, the entoptic picture of the yellow macula appears as a dark, oval shadow. Thus the picture of Maxwell's spot is produced by the diascleral method. In this case, the shadow is produced by absorption of the blue rays by the yellow material in the macula.

H. D. Lamb.

4

OCULAR MOVEMENTS

Bielschowsky, A. **Lectures on motor anomalies. 1. The physiology of ocular movements.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 843-854.

Guibor, G. P. **A classification of concomitant strabismus.** Arch. of Ophth., 1938, v. 19, June, pp. 947-958.

A classification of nonparalytic squint into seven groups is presented. The effects of orthoptic training on the various groups is discussed.

T. E. Sanders.

Krimsky, Emanuel. **Some newer developments in precision type stereoscopes.** Arch. of Ophth., 1938, v. 19, March, pp. 394-402.

Two stereoscopes designed by the author and illustrated by photographs are described. The senior or phorometric model is calibrated so as to enable the examiner to determine readily the divergence and convergence status of the eyes both at infinity and at any desired range of accommodation and thus to diagnose and classify the type and degree of muscle anomaly. He can determine the total range of fusion; the amount of vertical, rotary, or horizontal phoria; the measurement of false projection; lateral or vertical deviations; and prismatic vergence. The junior model is designed primarily for home training but serves as a diagnostic instrument, although less completely.

J. Hewitt Judd.

Marlow, F. W. **A tentative interpretation of the findings of the prolonged occlusion test on an evolutionary basis.** Arch. of Ophth., 1938, v. 19, Feb., pp. 194-204.

The phorias and ductions can all be accounted for on an evolutionary basis and represent incomplete development in the individual, as ontogeny tends to recapitulate phylogeny. The optic vesicles, which when first formed are direct-

ly opposite to one another, gradually turn forward so that by the end of the third month the optic axes of the respective eyes diverge 45 degrees from the midline, becoming parallel before birth. When this process is incomplete, exophoria with or without hyperphoria results, and when it is overdone esophoria with or without hyperphoria occurs. The findings in 700 cases tested by prolonged occlusion are summarized and suggestions made as to the best method of dealing with the conditions found. J. Hewitt Judd.

Ohm, J. **Nystagmus.** 44th contribution. **Congenital rotatory (rolling) nystagmus of the eyes.** Graefe's Arch., 1938, v. 138, pt. 5., pp. 693-721.

Physiologic rotation of the eyes is reflexively produced by stimulation of (1) the labyrinth, (2) the three superior cervical nerves, (3) the eyes; in the latter instance (a) as a tendency to an opposite rotation of the vertical meridian in the haploscope; (b) by optokinetic stimulus in the narrow sense, when the eye gazes at a rotating disc, furnished with white and black bands. In eyes with rotatory nystagmus, the axis of rotation would seem to pass through about the center of the pupil but definitely nasal from the fovea. Among 70 cases, the rotation was present in both eyes in 45 cases, or 64.3 percent. Both phases occurred with the same speed (were pendulum-like) in 35 cases, or 50 percent. The movement was with a jerk clockwise in 2 cases or 2.9 percent, counterclockwise in 6 cases or 8.7 percent. In 4 cases or 5.7 percent, one eye showed rotation while the other presented another kind of movement. The rotation was associated with horizontal movements in 21 cases or 30 percent, in both eyes at the same time in 17 cases or 24.3 percent. Of the 70 cases, squint was present in 43 or 61.4 percent. Of the latter, not less than 22 presented vertical divergence, in 20 cases combined with convergence. H. D. Lamb.

Parinaud, H. **Paralysis of associated movements of the eyes.** Ann. d'Ocul., 1938, v. 175, Jan., pp. 47-66. (See Section 18, Hygiene, sociology, education, and history.)

Smukler, M. E. **Simplification of the O'Connor cinch operation.** Arch. of Ophth., 1938, v. 19, June, pp. 930-935.

A modification of the technique of the O'Connor cinch operation is described. The needle is replaced by metallic cement forming a flexible metallic tip on either end of the strand. The ordinary hooks are replaced by grooved separators facilitating the handling of the muscle strands. T. E. Sanders.

Verhoeff, F. H. **Anomalous projection and other visual phenomena associated with strabismus.** Arch. of Ophth., 1938, v. 19, May, pp. 663-699.

Anomalous projection and retinal correspondence as related to strabismus are discussed in detail. The paper is not suitable for abstracting.

T. E. Sanders.

Vianna, A. M. **A case of convergent strabismus with apparent divergent strabismus in the deviating eye.** Ann. d'Ocul., 1938, v. 175, June, pp. 442-446.

The patient had a large angle gamma in the deviating eye which made it appear to diverge when the master eye was occluded. John M. McLean.

Wiedersheim, O. **Miners' nystagmus in the Saar coal region.** Graefe's Arch., 1938, v. 138, pt. 5, pp. 515-563.

In 1893 Hoederath of Saarbrücken

carried out for the first time conclusive observations on miners' nystagmus in the coal mines of the Saar. In the present article, Wiedersheim, after eighteen years activity with the miners' workgroups in the Saar, presents an exhaustive description of miners' nystagmus. The influence of psychic and nervous factors is very important. The author has observed no case where an injury to a miner at his work has resulted from the nystagmus. Accidents and debilitating diseases can bring out a previously latent nystagmus. The favorable effect upon the nystagmus of cessation from miner's work is well recognized. Nystagmus begins in miners generally between the ages of 26 and 45 years. Before appearance of the disorder they have as a rule been employed as miners from 11 to 30 years. The ages at which the majority of the sufferers first consult the eye physician lie between 40 and 55 years. Nystagmus is today just as prevalent among the coal miners of the Saar as 45 years ago. The percentage has always varied between 5 and 10 percent of the entire number of coal miners employed.

The movements of the eyeball with nystagmus are photographed on a cinema film. There is applied to the eyeball a dark-colored contact glass, provided with a peg, 1 cm. long, having a polished glistening knob on its end. The light reflected from the latter produces on the moving film a curved line, from which the character of the nystagmus and the number of oscillations per minute are ascertained. The various forms are described.

Where gas is greater in the mines, nystagmus is more commonly encountered. At considerable length, the author points out important measures to combat miners' nystagmus.

H. D. Lamb.

Zimmermann, H. E. **On results of functional treatment of strabismus in removal of amblyopia and restoration of binocular vision with prism spectacles.** Klin. M. f. Augenh., 1938, v. 100, April, p. 600.

Out of 150 cases of strabismus, 148 were considerably disturbed with regard to binocular vision, 68 especially so. In 46 out of 50 amblyopes with central fixation and 16 out of 18 with eccentric fixation complete cure of squint amblyopia was obtained by bandaging the leading eye and by stereoscopic exercises. Out of 93 cases in which at first there was no binocular fusion or perception of depth in spite of prisms, and out of 55 who originally had only binocular fusion, 46.6 percent completely regained binocular vision with perception of depth. Twenty-five percent finally had only binocular fusion without perception of depth.

C. Zimmermann.

5

CONJUNCTIVA

Berger, A. R., Goldstein, D. H., McEwen, C., and Alexander, R. C. **Conjunctivitis associated with infection by streptococcus viridans.** Arch. of Ophth., 1938, v. 20, July, pp. 19-29.

Streptococcus viridans was apparently the causative organism of an epidemic of 35 cases of acute conjunctivitis in a boys' camp. The disease was of a purulent type, of varying severity, and had a period of incubation of from 16 to 24 hours and an average duration of 7 days. Treatment apparently did not alter the course and there were no significant complications. An immunologic identity was demonstrated between two strains recovered from the epidemic in Pennsylvania and one from an epidemic in Vermont.

J. Hewitt Judd.

Bertoldi, Maria. **Treatment of trachoma with benzylcinnamic ether.** Rassegna Ital. d'Ottal., 1938, v. 7, Jan.-Feb., p. 89.

The combination of cinnamic acid and benzyl alcohol was introduced by Jacobson for the treatment of trachoma in 1932. Bertoldi employed this treatment in 25 cases, and obtained marked improvement in 11, slight improvement in 7, and no change in 5, while 2 appeared to be made worse. He concludes that it offers its greatest advantage in subjects affected with cicatricial trachoma, especially in the stage of recurrence with intense photophobia, corneal complications, and bulbar inflammation. Eugene M. Blake.

Blobner, Ferdinand, **Crystalline degeneration of conjunctiva and cornea.** Klin. M. f. Augenh., 1938, v. 100, April, p. 588.

A bricklayer of 45 years gave a history that twenty years previously hot ashes had fallen into both eyes. He always saw well until in June, 1935, he observed sudden diminution of sight with presbyopia and hemeralopia. Cornea and conjunctiva of each eye presented glittering opacities consisting of innumerable minute iridescent and densely crowded accumulations of crystalline aspect reaching as far back as Descemet's membrane. Corneal sensibility was normal and fluorescein did not stain the cornea or conjunctiva. A similar case has never been described. C. Zimmermann.

Bowing, H. H., and Fricke, R. E. **The radium treatment of vernal conjunctivitis.** Amer. Jour. of Roentgenology and Radium Therapy, 1937, v. 38, Nov., p. 740.

The authors report their studies and give a brief analysis of cases seen between 1931 and 1935, during which time 23 were treated with radium. Radium treatment is effective in most cases. The disease demands two or three cautious applications at intervals of a few months. Where the bulbar conjunctiva is involved, the results are often not so good. Since the disease is benign and will heal spontaneously after a few years, great care should be used to avoid injury. F. M. Crage.

Busacca, Archimede. **A modification of MacReynold's pterygium operation.** Ann. d'Ocul., 1938, v. 175, June, pp. 454-457.

The variations from MacReynold's technique consist essentially of shaving off the deeper layers of the pterygium, making a hole at the base to avoid distortion of the caruncle, and leaving a large area of bare sclera which must be covered with ointment and a pad for ten to twelve days before it heals. Recurrences have followed this operation. John M. McLean.

Cramer, I. I. **Oculoglandular tularemia.** Arch. of Ophth., 1938, v. 20, July, pp. 88-89.

A boy aged sixteen years developed a typical case of oculoglandular tularemia by rubbing an irritated eye with hands contaminated by an infected rabbit. Typical, small, shallow ulcers developed on the lower palpebral conjunctiva. An apparently rare complication in this case was the appearance of an ulcerated process in the pharynx during the progress of the disease. Clinically, the ulcers closely resembled those seen on the conjunctiva. It is suggested that contamination of the throat occurred via the lacrimal duct. (Photograph.) J. Hewitt Judd.

Fernandez, L. J., and Fernandez, R. F. **Sulfanilamide in gonorrheal ophthal-**

mia. Amer. Jour. Ophth., 1938, v. 21, July, pp. 763-766.

Julianelle, L. A. **Studies on the pathogeny of trachoma.** Brit. Jour. Ophth., 1938, v. 22, June, pp. 336-343.

The causative factors of diet, bacteria, and virus in relation to trachoma are discussed. The author accepts the tendency to regard the disease as an infection due to a virus. (Bibliography.)

D. F. Harbridge.

Julianelle, L. A., and Lange, A. C. **Studies on inclusion blennorrhea. 1. Clinical and general observations.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 890-904.

Morax, Victor. **Gonococcic infection.** Annal. d'Ocul., 1938, v. 175, Jan., pp. 89-132.

This article forms a part of a work on ocular bacteriology which the author left almost completed at the time of his death and which will be published soon. It is an exhaustive textbook study of the subject as related to the eye. (4 color-photographs.)

Poleff, M. **New methods in contemporary experimental trachomatology.** Arch. d'Opht. etc., 1938, v. 2, June, p. 517.

The existence of rickettsioid corpuscles in trachoma has been demonstrated. Thanks to the experimental work of Szily (confirmed by the author), the virus has been cultivated in vitro by injecting the corpuscles into the vitreous of rabbits. An intraocular folliculosis leading to cicatrization is produced. Intratesticular inoculation of trachoma corpuscles in guinea pigs has produced a pure culture of the corpuscles, corresponding to the descriptions of Busacca and Cuénod. (Bibliography, illustrations.) Derrick Vail.

Sezer, F. N. **Accidental vaccination of the conjunctiva.** Arch. of Ophth., 1938, v. 20, July, pp. 89-91.

A case of a boy, aged 8 years, is reported in which the infection evidently took place from the vaccination vesicles of his brother. Photographs show the boy before and after treatment with 30-percent mild protein silver and a solution of an acridine derivative. The eye healed, leaving a symblepharon, entropion, and defects on the ciliary margin.

J. Hewitt Judd.

Thygeson, Phillips. **Problem of rickettsias in trachoma.** Arch. of Ophth., 1938, v. 20, July, pp. 16-18.

The formations which have been described by Busacca and Cuénod and Nataf as rickettsia-like bodies occurring in large numbers in the trachoma follicles are not parasitic but in all probability cell granules and cytoplasmic débris. No minute parasitic bodies other than the elementary and initial bodies of the epithelial cell inclusions of trachoma could be demonstrated in trachomatous material from Tunis, Brazil, and the United States.

J. Hewitt Judd.

6

CORNEA AND SCLERA

Kalaschnikov, W. **The use of eserine in the treatment of keratitis.** Ann. d'Ocul., 1938, v. 175, May, pp. 396-401.

The author believes that eserine is more efficacious than atropine for corneal affections. He cites Katz's rule, "for iritis atropine, for keratitis eserine." Only weak solutions (0.1 to 0.5 percent) should be used. Nine cases are reported in which keratitis cleared up under eserine. There were two of hypopyon ulcer, one of phlyctenular keratitis, one of superficial keratitis second-

ary to purulent conjunctivitis, one syphilitic, one eczematous, one traumatic, one following cataract extraction, and one undescribed.

John M. McLean.

Klein, M. **Experimental data on the problem of permeability of the cornea.** Brit. Jour. Ophth., 1938, v. 22, July, pp. 401-408.

Experiments on excised pigs' eyes and living rabbits' eyes with iodide and nitrite are described, to demonstrate the importance of the permeability of the cornea. It is suggested that, iodide and nitrite not being found in the body under normal conditions, the cornea would show a different reaction to ions normally present. The experiments were therefore repeated with special apparatus dealing with ions normally found and these findings appear in the paper written by the author in collaboration with Sarkany, and abstracted below. (Tables, references.)

D. F. Harbridge.

Klein, M., and Sarkany, J. **Experimental data on the problem of the permeability of the cornea.** Brit. Jour. Ophth., 1938, v. 22, July, pp. 409-417.

The permeability of the excised cornea with respect to water and chloride ions was studied. The conclusions are that a flow of water through the cornea is possible, that this permeability exists in a reverse direction as well as in the epithelial-endothelial direction, and that under osmotic pressure chloride ions can diffuse in each direction to the opposite surface. (Tables.)

D. F. Harbridge.

Niemeyer, Waldemar. **A case of trachomatous deep interstitial keratitis.** Rev. de Oft. de São Paulo, 1938, v. 6, Jan.-Feb.-March, pp. 25-28.

In a man of sixty years, the left eye (the right being perfectly healthy) showed deep nodular infiltration of the cornea, with vessels in the subepithelial layer and also in the deeper layers, but without characteristic pannus and without any affection of the corneal limbus. The infiltrations had the size of conjunctival follicles. The conjunctivas gave no sign of involvement, although a conjunctival scraping, stained with Giemsa, showed some apparent trachoma corpuscles. Under antitrachomatous treatment ("partly mechanical and partly hemotherapeutic"), not described in detail by the author, the vision rose in the course of six months from 5/20 to 5/6. The patient dated his disturbance from a slight wound by a dry hard leaf fifteen days before onset.

W. H. Crisp.

Zentmayer, William. **Association of an annular band of pigment on posterior capsule of lens with a Krukenberg spindle.** Arch. of Ophth., 1938, v. 20, July, pp. 52-57. (See Section 9, Crystalline lens.)

7

UVEAL TRACT, SYMPATHETIC DISEASE, AND AQUEOUS HUMOR

Coppez, H., and Dujardin, B. **A case of Besnier-Boeck disease or benign lymphogranulomatosis of Schaumann with ocular manifestations.** Arch. d'Opht. etc., 1938, v. 2, June, pp. 497-505. (See Amer. Jour. Ophth., 1938, v. 21, July, p. 808.)

8

GLAUCOMA AND OCULAR TENSION

Blaess, M. J. **A further report on the seton operation in glaucoma.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 865-870.

Magitot, A. **Glaucoma without hypertension.** Ann. d'Ocul., 1938, v. 175, May, pp. 349-368.

In the group of glaucomas without hypertension, Magitot isolates three clinical types. In the first category, he places certain forms of glaucoma arising in myopic eyes. These cases are compensated glaucoma in myopes with low tension and excavation of the discs. In the second are cases of chronic glaucoma with tension scarcely higher than normal but usually higher in one eye than the other. The tension may remain within normal limits for long periods before any definite symptoms appear. There may be little excavation but provocative tests are usually positive. In the third group are the atrophies with excavation which must be classed as non-glaucomatous. These cases may be due to chiasmal pressure, or to sclerosis of the nutrient vessels. He does not believe that there is conclusive evidence to support the suggestion of pressure from sclerosed carotids.

John M. McLean.

9

CRYSTALLINE LENS

Bellows, J., and Rosner, L. **Biochemistry of the lens. 11. Effect of galactose on permeability of the capsule of the lens.** Arch. of Ophth., 1938, v. 20, July, pp. 80-84.

Investigations were conducted on the effect of galactose and dextrose on the permeability of the capsule of fresh beef lenses. Galactose caused a marked decrease in the capsular permeability and dextrose produced a similar effect, but to a lesser extent. The authors discuss the significance of these findings in relation to galactose cataract in rats and diabetic cataract in human beings.

J. Hewitt Judd.

Cornet, Emmanuel. **A safety suture for intracapsular extraction.** Ann. d'Ocul., 1938, v. 175, April, pp. 322-324.

Description of a complicated corneoepiscleral suture to be tightened by the assistant during delivery of the lens. It is supplemented by five conjunctival-flap sutures. (2 illustrations.)

John M. McLean.

Gailey, W. W. **Some problems encountered in cataract surgery.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 855-864.

Gallenga, Riccardo. **Cataract extraction in congenital aniridia.** Rassegna Ital. d'Ottal., 1938. v. 7, March-April, p. 168.

Gallenga discusses the various operative approaches to the question of extraction of cataract in congenital aniridia and gives the indications for operation. He reports a case successfully operated upon, in a man of 22 years, with immature subluxated cataract, tension slightly elevated, and nystagmus. A discission was performed and, since swelling of the lens proceeded slowly, extraction was done eight days later. A bridge flap, with two sutures placed before section, made the extraction safer, and credit is given to akinesia and deep orbital injection. The final vision was 1/10, but the tension was slightly higher than before operation.

Eugene M. Blake.

Grosz, Emile de. **A few words on the technique of intracapsular cataract extraction.** Ann. d'Ocul., 1938, v. 175, April, pp. 320-322.

On the basis of thirty years of cataract operations and some 30,000 cases from his clinic, Grosz defends the "Hungarian method" of direct intracapsular extraction against St. Martin's

arguments for the tumbling operation. Of 10,000 lenses about eighty percent were successfully extracted in capsule. Vitreous loss was about 4 percent but has been reduced to a lower figure since the introduction of retrobulbar injection. Akinesia, retrobulbar injection, and superior-rectus fixation are all important factors in successful intracapsular extraction. A round pupil is unquestionably desirable but not so safe as iridectomy. Direct extraction is easier than tumbling and a safer operation for the average surgeon.

John M. McLean.

Magitot, A., and Dubois-Poulsen, A. **Treatment of iris prolapse with trichloracetic acid.** Ann. d'Ocul., 1938, v. 175, June, pp. 449-454.

The authors heartily endorse the method described by Bettman and Barkan (see Amer. Jour. Ophth., 1937, v. 20, p. 131) for treatment of iris prolapse by repeated cauterizations with trichloracetic acid. Eleven illustrative cases are reported.

John M. McLean.

Margenat, J. **Phacoërisis.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1936, v. 1, pp. 223-226.

The author advocates Barraquer's technique for extraction of cataract, although he admits that it requires more dexterity than other methods. The technique is described in detail.

Ramon Castroviejo.

Rezende, Ciro de. **Trials of ocular biomicroscopy after intracapsular cataract extraction.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1906, v. 1, pp. 215-219.

The author has studied with the slit-lamp cases of cataract extraction by intracapsular methods. In a number of them the vitreous protruded through the pupil into the anterior chamber. If the so-called hyaloid membrane is preserved, the hernia of vitreous into the anterior chamber is called "simple" by the author. If the hyaloid membrane is broken, and the vitreous is free in the anterior chamber, the author calls the hernia "complicated." A brief discussion is given to deviation of the pupil after intracapsular cataract extraction. (Bibliography.) Ramon Castroviejo.

Tainter, M. L., and Borley, W. E. **Influence of vitamins and dinitrophenol on the production of experimental cataract.** Arch. of Ophth., 1938, v. 20, July, pp. 30-36.

Experiments on rats and guinea pigs to produce cataractous changes in the lens with dinitrophenol and deficiencies of vitamins A, B2, or C were uniformly unsuccessful. Dinitrochlorobenzene, a theoretically possible contaminator of commercial dinitrophenol, and toluquinone, the sole compound to which one patient with cataract was exposed, were both fed to rats without producing demonstrable lenticular changes. In essence, the procedure used consisted of creating by means of diet, vitamin A, B2, or C deficiency and determining whether or not the addition of dinitrophenol to the diet led to a greater tendency to cataractous changes. The details of the methods are given in connection with a discussion of the results in each type of vitamin deficiency. J. Hewitt Judd.

Taube, E. L. **Cataract extraction in subclinical scurvy.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 910-911.

Terry, T. L. **A modified corneal clamp to facilitate the insertion of stitches.** Arch. of Ophth., 1938, v. 20, July, pp. 91-94.

This instrument was devised to approximate the edges of a corneal or corneoscleral wound and thus facilitate the insertion of stitches. Verhoeff's instrument has been modified so as to be opened and closed in the manner of ordinary tissue forceps. The upper plate of the clamp is curved on the under surface, and the flat portion of the clamp, the foot plate, presses the cornea against the upper concave surface, holding the two edges of the cornea as firmly as the needle point of the Verhoeff instrument. This instrument may be slipped from side to side obviating the necessity of completely removing the clamp and reinserting it for each stitch. The instrument is shown by drawings. J. Hewitt Judd.

Yudkin, A. M. **Diet and vitamins in relation to cataract.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 871-881.

Zentmayer, William. **Association of an annular band of pigment on posterior capsule of lens with a Krukenberg spindle.** Arch. of Ophth., 1938, v. 20, July, pp. 52-57.

A boy aged sixteen years presented this unusual condition. The annular bands of pigment on the posterior capsule of the lens were probably due to the maintenance of contact between the tips of the ciliary processes and the lens for too long a period and were formed of pigment detached from the ciliary processes when they finally separated. The author feels that the Krukenberg spindle is formed from granules freed from the pigment line and carried by the circulation of the aqueous into the anterior chamber where the thermal currents deposit them on the posterior surface of the cornea. The article is illustrated by drawings.

J. Hewitt Judd.

10

RETINA AND VITREOUS

Bietti, Giambattista. **Some atypical or rare forms of retinal degeneration.** Boll. d'Ocul., 1937, v. 16, Dec., pp. 1159-1244.

The author describes numerous cases of degeneration of the external layers of the retina. Among these is a case of atypical retinitis pigmentosa with the characteristic pigment changes only in the lower nasal quadrants, no hemeralopia and no contraction of the visual fields, in a deaf-mute girl of 25 years born from first-cousin parents. Atypical retinitis pigmentosa occurred in boys of seven and eight years affected by congenital lues with typical and atypical Lawrence-Biedl syndrome. Retinitis pigmentosa with poor pigment was seen in a girl of eighteen years affected by psychic disturbances and an adiposogenital syndrome. Senile atypical forms of retinitis pigmentosa occurred in a woman of 68 and a man of 85 years. Other cases include: four of retinitis punctata albescens with peripheral pigmentation; one of gyrate atrophy of choroid and retina; one of progressive familial degeneration of the macula, with equatorial pigment changes, in a man of 49 years; eight of infantile (juvenile and adult) macular degeneration with concomitant retinitis pigmentosa or other degenerative changes. The writer divides the cases of tapetoretinal degeneration into (1) a group having peripheral localization with a tendency to generalization, (2) a group with central localization and a slight tendency to generalization with or without nervous or psychic disturbances, and (3) a group of tapetoretinal degeneration accompanied by symptoms of amaurotic family idiocy of Spielmeyer-Vogt, that is, related to degeneration of

internal layers or without a particular familial character. (Bibliography, 20 figures.) M. Lombardo.

Bistis, J. **Obliteration of the retinal arteries and retinal arterial hypertension.** Ann. d'Ocul., 1938, v. 175, June, pp. 447-448.

Retinal arterial hypertension is found in general hypertension, albuminuric retinitis, diabetic retinitis, and syphilis. Bailliart has described local arterial hypotension in cases of partial occlusion of the central retinal artery. A case is reported in which occlusion of the superior temporal branches was accompanied by a rise in pressure instead of a fall. The patient had generalized arteriosclerosis. John M. McLean.

Dax, E. C. **A melanosome-dispersing substance in the blood and urine of patients with retinitis pigmentosa.** Brit. Jour. Ophth., 1938, v. 22, June, pp. 345-352.

In July, 1937, the author essayed a classification of cutaneous pigmentation. Samples of urine from selected cases and later from pregnant women were used in the work, and frogs and toads were used for experimental purposes. The complete method used is described. It is the opinion of the author that the evidence suggests a pituitary origin for the cases of retinitis pigmentosa described. (References, illustrations.) D. F. Harbridge.

Girardet and Jacot. **A retinal tear bordering on the disc.** Ann. d'Ocul., 1938, v. 175, May, pp. 402-405.

A retinal tear about 2 mm. long, just nasal to the disc, over an area of myopic conus, was treated successfully by diathermy. Detachment had been feared but was prevented, with retention of the existing visual acuity. The optic nerve bore the adjacent trauma well. John M. McLean.

Goar, E. L. **Angioid streaks in the ocular fundus with traumatic rupture of the choroid.** Amer. Jour. Ophth., 1938, v. 21, Aug., pp. 907-910.

Meyer, Correa. **External exudative hemorrhagic retinitis of Coats.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1936, v. 1, pp. 179-184.

The author discusses at length the pathologic anatomy, etiology, diagnosis, prognosis and treatment of Coats's retinitis. Ramon Castroviejo.

Spinola, Colombo. **Retinal arterial pressure in rhinopathies.** Trabalhos do Primeiro Cong. Brasileiro de Ophth., 1936, v. 1, pp. 195-200.

After discussing briefly the different methods used to measure the retinal blood pressure, the author gives his experience with the use of the ophthalmodynamometer of Bailliart. The author has arrived at the following conclusions: (1) There is a certain relation between the rhinopathies and arterial blood pressure. (2) Most of the nasal affections are manifested by minimum and maximum hypertension of retinal blood pressure. (3) In atrophic rhinitis, such as ozena, the retinal pressure is slightly lowered. (4) After surgical intervention in the nose there is also a diminution of retinal arterial pressure. Ramon Castroviejo.

11

OPTIC NERVE AND TOXIC AMBLYOPIAS

Adamantiadis, A. **Two cases of recurrent retrobulbar neuritis.** Ann. d'Ocul., 1938, v. 175, June, pp. 432-441.

A syphilitic patient had eight recur-

rences of retrobulbar neuritis in fourteen years. Antisyphilitic treatment did not influence the course or recurrence of the nerve lesions but did control two intercurrent attacks of iritis. Another patient who had signs of old tuberculosis and "probable" syphilis had seven recurrences of retrobulbar neuritis in ten years. It is suggested that epidemics of grippe were responsible for the recurrences in already diseased tissues. John M. McLean.

Bollack, J., Delthil, S., and Offret, G. **A particular form of unilateral optic neuritis.** Ann. d'Ocul. 1938, v. 175, June, pp. 421-432.

Three cases are reported, each with lower-segment field-defect in one eye only, slight edema of the disc margins with small hemorrhages, and preservation of central visual acuity. None had sinus disease, syphilis, or general neurologic changes, although two of the three had slight pupillary inequality with intact reflexes. Onset was marked by vague peripheral visual disturbances discovered by the patient. At the end of several months the field defect was not altered but pallor of the disc was evident.

Apparently the patients had no other evidence of neurologic disease, intracranial tumor, orbital tumor, vascular lesion, or meningitis. Therefore the authors believe they have a new form of segmentary optic neuritis.

John M. McLean.

Calderin, C., Scull, L., Montero, R., and Garcia, A. **Crouzon's disease in a female negro child.** Rev. Cubana Oto-Neuro-Oft., 1937, v. 6, Nov.-Dec., p. 131.

The authors describe a case of Crouzon's disease, or cranio-facial dysostosis (hitherto reported only among the French or their descendants) in a negro child of twelve years. While the familial character of the case is not definitely established, it is believed to belong to the hereditary form of the disease. Dystocia with symphysiotomy and hereditary lues are reported in the anamnesis. Cranial deformation was first noted at the age of ten months. The relevant ocular findings were: exophthalmos, divergence, nystagmoid twitchings, high myopia, optic atrophy, and chorioretinitis with small retinal tears. The cause of the optic atrophy is believed not to be due to papilledema but to compression of the optic nerves at the anterior orifice of the optic foramina, and the advisability of their surgical decompression is suggested. (Illustrated.) M. Davidson.

13

EYEBALL AND ORBIT

Fonseca, A., and Tolosa, A. **Exophthalmos in hypophyseal dysostosis or Schüller-Christian disease.** Rev. de Oft. de São Paulo, 1938, v. 6, Jan.-Feb.-March, pp. 5-12.

The patient was a girl of six years. There was marked exophthalmos, greater on the right side. As shown by X-ray, there were areas of bone destruction in the cranial vault, affecting all the bony layers. The orbits shared in this process. There was considerable enlargement of the sella turcica. The intracranial tension was increased. The Wassermann test was negative. Withdrawal of the child from the hospital made it impossible to observe the effect of deep radiotherapy, which is recommended for such cases. W. H. Crisp.

Motolese, Alfonso. **The pathogenic action of Bacillus pyocyaneus on ocular tissues of the rabbit.** Boll. d'Ocul., 1937, v. 16, Dec., pp. 1245-1251.

In the right eyes of sixteen rabbits the author used an emulsion of germs obtained from a 24-hour agar culture and diluted in physiologic salt solution. In one group of rabbits he abraded the corneal epithelium, instilled two drops of the emulsion in the conjunctival sac, and closed the lids by sutures. The cornea was found reëpithelized and no damage to the eye was noticed. In a second group of rabbits 1/40 c.c. of emulsion was injected in the cornea; in a third group 1/10 c.c. was injected in the anterior chamber; and in a fourth group the same dose was injected in the vitreous. In all these three groups the eyes were destroyed by panophthalmitis. A histologic description of these eyes is given. These provoked infections followed the usual course of spontaneous infections in human patients. (Bibliography, 2 figures.)

M. Lombardo.

Recordon, E., and Griffiths, G. M. **A case of bilateral anopthalmia (clinical and histological report).** Brit. Jour. Ophth., 1938, v. 22, June, pp. 353-360.

A male child born on November 13, 1935, appeared normal except for the one defect, but declined, and died on January 8, 1936. There was no history of abnormality in the family, and no consanguinity; and a normal child has since been born. Post-mortem findings are presented in full. It is maintained that this is a proved case of bilateral primary anophthalmia, with complete failure in development of the optic vesicles. It is not to be confused with cases of "degenerative" or "consecutive" anophthalmia. A brain teratoma and a patent foramen ovale were the only other abnormalities noted. (Figures, references.) D. F. Harbridge.

Tommasini-Mattiucci, A. **Unilateral exophthalmos from neoplasm of the middle cranial fossa.** Boll. d'Ocul., 1938, v. 16, Dec., pp. 1252-1267.

For about six years a woman aged fifty years had shown some protrusion of the left eye. Recently the protrusion had become more manifest and had been accompanied by headaches diffused throughout the head but the intensity of which decreased during rest in bed. The sight gradually diminished and diplopia manifested itself in looking upward. X-ray examination showed partial destruction of the upper external margin of the orbit, the external wall of the orbit, and a zone of the frontal and temporal bones. After opening the orbit by Krönlein's method a yellowish mass was excised. It appeared to originate from the great wing of the sphenoid and was diagnosed as a cholesteatoma. The surgical treatment, ocular symptomatology, and genesis of the neoplasm are discussed. (Bibliography, 6 figures.) M. Lombardo.

14

EYELIDS AND LACRIMAL APPARATUS

Cossu, Giovanni. **A case of palpebromandibular synergy (Marcus Gunn).** Rassegna Ital. d'Ottal., 1938, v. 7, March-April, p. 211.

The author describes a case of associated lid-jaw movement in a nineteen year-old boy, a Grandmont ptosis operation being performed but with no benefit. He discusses all of the explanations which have been offered of Gunn's phenomenon, but does not express a preference for any. (3 figures.)

Eugene M. Blake.

NEWS ITEMS

Edited by Dr. H. Rommel Hildreth
640 S. Kingshighway, Saint Louis

News items should reach the Editor by the twelfth of the month

Deaths

Dr. Walter Karl Seelye, Seattle, Washington, died June 24, 1938, aged 70 years.

Dr. George Foster Gourley, Steubenville, Ohio, died June 28, 1938, aged 59 years.

Dr. John Robert Wilson, Bennington, Vermont, died June 28, 1938, aged 58 years.

Dr. Charles C. Stephenson, Los Angeles, died June 12, 1938, aged 74 years.

Dr. Alfred Edward Maumenee, Birmingham, Alabama, died June 5, 1938, aged 58 years.

Dr. James A. Bline, Yakima, Washington, died about July 20, 1938.

Miscellaneous

A number of copies of the January, 1937, issue of this Journal are in demand. The Journal will pay $1.25 per copy.

The Thirteenth Annual Spring Graduate Course in Ophthalmology and Otolaryngology will be given at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Virginia, April 3 to 8, 1939.

Societies

On March 22, 1938, the Ophthalmological Society of Australia (B.M.A.) was organized. The officers are: president, Sir James W. Barrett; vice-president, Dr. A. James Flynn; secretary, Dr. Darcy A. Williams; treasurer, Dr. Leonard J. C. Mitchell. The first meeting will be held at Melbourne, April 3 to 6, 1939.

The Twenty-third International Medical Assembly, Inter-State Postgraduate Medical Association of North America, will meet in Philadelphia, October 31, November 1, 2, 3, 4, 1938. The Joseph Schneider Foundation presentation this year will be given by Dr. Walter I. Lillie. His subject will be, "The clinical significance of retinal changes in arterial hypertension."

Personals

Dr. James Thompson, a former resident of Yakima, has taken over the practice of Dr. James A. Bline, who died in July, 1938, in Yakima.

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FIG 1

FIG 2

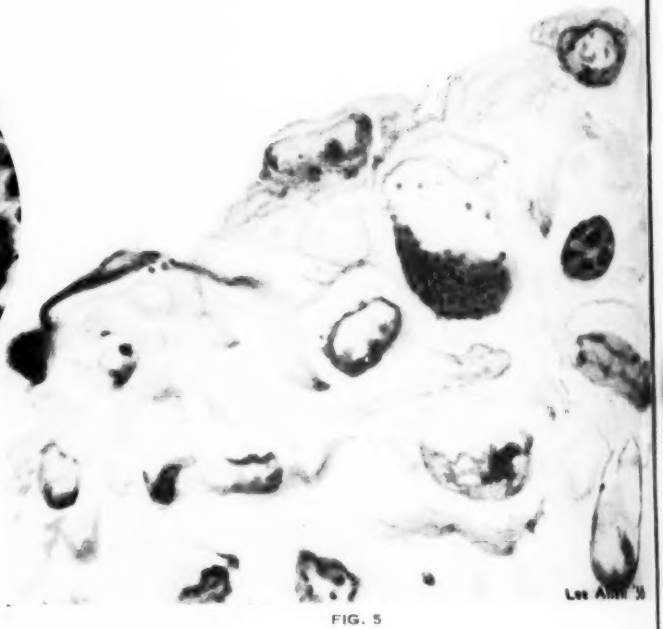

FIG. 5

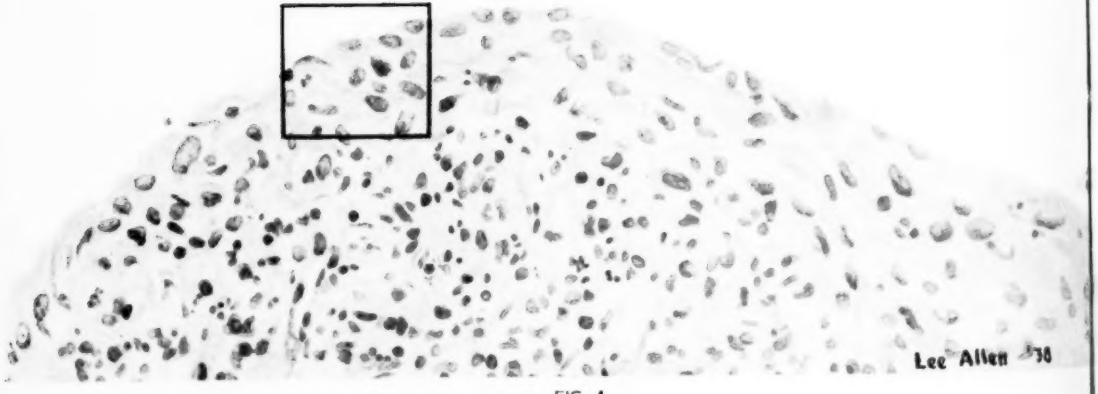

FIG 4